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# MALARIA
## and its Treatment

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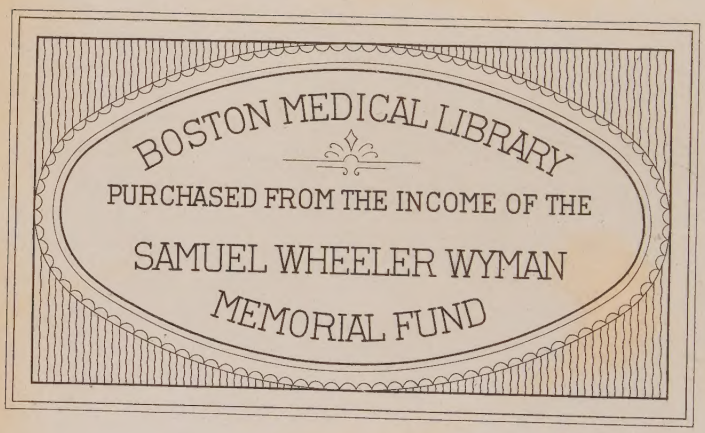
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# MALARIA AND ITS TREATMENT

## In the Line and at the Base

BY

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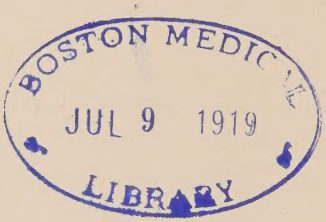

TO

MY FRIEND AND COLLEAGUE

SIR JAMES PURVES STEWART, K.C.M.G., C.B.;

SENIOR PHYSICIAN TO THE WESTMINSTER HOSPITAL;

HON. COLONEL ARMY MEDICAL SERVICE;

FOR THE SYMPATHETIC INTEREST HE TOOK IN MY WORK,

AND THE ENCOURAGEMENT AND ASSISTANCE

HE GAVE ME DURING THE TIME

HE WAS CONSULTING PHYSICIAN TO THE

BRITISH EXPEDITIONARY FORCE

IN SALONIKA.

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# PREFACE.

IT is extremely difficult to deal with a subject as controversial as Malaria, and, at the same time, avoid treading upon other people's toes. Opinions and shades of opinion in regard to it are as diverse as the colours of the flowers in the Struma Valley in Spring, or as the tints of the Macedonian Hills on the Monastir front.

My aim throughout has been to use the simplest language possible, to be concise, and—while going into the most minute descriptions when necessary—to avoid the error so common in scientific works, of forcing the reader to wade through a mass of unimportant detail before reaching the point—which even then is apt to be obscure. In doing this I have kept in view the requirements of the busy general practitioner, and, by including numerous illustrations, have endeavoured to make it possible for the average layman, who has suffered from Malaria, to read with interest and to understand my arguments.

I do not claim that all my opinions are correct; I merely state exactly what I found.

The case-sheets given are accurate even to the hours at which the drugs were administered. I have confessed to my failures and recorded my successes. It is quite easy for the student to draw his own conclusions from the data given.

If I appear to be dogmatic, and if the eternal "Ego"

is, perhaps, more in evidence than modesty permits of, I apologise. In extenuation, however, I must point out that I have had little or no access to the literature on the subject and have had to rely on my own observations, experiences and knowledge. My excuse for any shortcomings in the expression of my ideas and the arrangement of the book is that it was written under active service conditions—partly at the Base, when, as Officer in Charge of the Medical Division of a great General Hospital, with an average of a thousand occupied beds under my care, I was subjected to constant interruptions, and partly at the Front, where, as a Regimental Medical Officer, or an M.O. of a Field Ambulance, I have had to do my writing, under adverse conditions, in a dugout or a tent.

My cordial thanks are due to Lieutenant R. Robertson, R.A.M.C., who had charge of my intravenous wards, and also to Lieutenant J. A. Currell, R.A.M.C. The excellence of the work of these medical officers, the care and trouble they took, together with the accuracy of their notes, made it possible for me to obtain the results which alone justified the writing of this book. I have also to thank Captain T. Ruddock West for the drawings of Malaria parasites, &c., Captain Jimmy Steele, R.A.M.C., and Lieutenant W. Anderson, R.A.M.C., for careful observation and notes on cases under their charge; Staff Sergeant Beesley, R.A.M.C., for the charts showing admissions and discharges (see Appendix) and the other Medical Officers, Sisters, and V.A.D.s of the old 28th General Hospital who by their work in the wards assisted and encouraged me.

I am also greatly indebted to Private T. Hustler—the Yorkshire artist—for the excellent coloured drawings of mosquitoes, &c., to Captain J. T. Carson, R.A.M.C.,

radiographer for assistance with the photographs, to Captain W. L. Millar, of the 41st General Hospital, and to the publishers, Messrs. John Bale, Sons and Danielsson, Ltd., for their helpfulness in the preparation of this volume.

I regret that some of my best photographs of anti-malaria work, &c., on the Balkan Front have not arrived in England. The loss of these is probably due to enemy action at sea, and unfortunately I am unable to replace them.

A. Cecil Alport.

*Macedonia.*

# CONTENTS.


PAGE

CHAPTER I.

Malarial Fever ... ... ... ... ... ... 1

CHAPTER II.

Prophylaxis ... ... ... ... ... ... ... 16

CHAPTER III.

Clinical Features of Acute Malaria ... ... 26

CHAPTER IV.

The Treatment of Malaria ... ... ... ... 35

CHAPTER V.

Routine Treatment of Malaria, and Cerebral Malaria ... ... ... ... ... ... 55

CHAPTER VI.

Pernicious Malaria with Cardiac Symptoms and Collapse ... ... ... ... ... ... 102

CHAPTER VII.

The Treatment of Chronic Malaria... ... ... 126

CHAPTER VIII.

Malarial Anæmia ... ... ... ... ... ... 140

CHAPTER IX.

PAGE

Pernicious Anæmia and Malaria ... ... ... 159

Malarial Cachexia.

CHAPTER X.

Blackwater Fever ... ... ... ... ... 180

CHAPTER XI.

Post-malarial Nervous Manifestations ... ... 240

CHAPTER XII.

Concurrent Diseases and Differential Diagnoses 249

Malaria and Appendicitis.

# ILLUSTRATIONS.


PAGE

Anopheles mosquito. Culex mosquito ... ... ... 3

Anopheline and culicine larvæ and pupæ ... ... 4

Preparation of a blood-film ... ... ... ... 13

Camp bed, with sand-fly and mosquito-proof curtain in position ... ... ... ... ... ... ... 17

Canal between Sorovitch and Lake Petrescoe, Macedonia 20

Cut section of brain in cerebral malaria ... ... .. 31

Medical Officer giving an intramuscular injection ... 45

An intravenous injection of quinine ... ... ... 45

Lumbar puncture: Direct method ... ... ... 54

,, ,, Indirect method ... ... ... 54

Case 2.—Saddler G. After recovery from cerebral malaria 76

Case 5.—Sergeant G. After recovery from cerebral malaria ... ... ... ... ... ... ... 76

Case 6.—Pioneer R. After recovery from cerebral malaria ... ... ... .. ... ... ... 84

Case 7.—Driver S. After recovery from cerebral malaria 84

Case 8.—Driver D. ,, ,, ,, ,, 91

Well-marked Kernig's sign in cerebrospinal meningitis 91

Cerebral malaria cases. After recovery. Case 10. Sergeant C. in bed ... ... ... ... ... 99

Three patients after recovery from cerebral malaria ... 99

Case 4.—Private R. Bilious remittent fever ... ... 123

Case 4.—Private R. After recovery from bilious remittent fever ... ... ... ... ... ... 123

PAGE

The evacuation of malaria cases on the Vardar Front ... 134

At an advanced dressing station.
Crossing a rough mountain pass.
Travois conveying a lying case over bad ground to an advanced dressing station.
Wheeled stretcher, Mark 1

Case 1.—Sergeant M. Blackwater fever and quinine amblyopia ... ... ... ... ... ... 191

Medical Officer giving an intramuscular injection ... 191

Case 4.—Private H. The acute stage of an attack of blackwater fever ... ... ... ... ... 210

Case 5.—Private W. The acute stage of blackwater fever ... ... ... ... ... ... ... 210

Case 2, Private E.; Case 4, Private H.; Case 5, Private W. After recovery from blackwater fever 212

Stegomyia mosquito ... ... ... ... ... 248

## Coloured Plates.

*Plasmodium malariæ*, parasite of quartan fever ... ... 8

„ composite field ... ... ... ... 8

*P. vivax*, parasite of benign tertian fever... ... ... 8

„ composite field ... ... ... ... ... 8

*P. falciparum*, parasite of malignant tertian, sub-tertian, or æstivo-autumnal fever ... ... ... ... 8

*P. falciparum*, composite field ... ... ... ... 8

Section of kidney in a case of blackwater fever... ... 182

Specimens of urine in blackwater fever ... ... ... 194

# MALARIA AND ITS TREATMENT IN THE LINE AND AT THE BASE.

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## CHAPTER I.

## MALARIAL FEVER.

MALARIA is the name given to a specific infective fever caused by the presence of three distinct species of protozoan parasites in the blood of man.

These parasites are :—

(*a*) The *Plasmodium malariæ* (quartan malaria).

(*b*) The *Plasmodium vivax* (benign tertian malaria).

(*c*) The *Plasmodium falciparum* (malignant tertian malaria).

HISTORY.—Hippocrates, the Father of Medicine, in the fifth century B.C., was the first to draw attention to tertian and quartan malaria, and described the intermittent nature of the fever associated with these conditions.

The name malaria, meaning "bad air," was, however, only given to the disease at a much later date by the Italians, who, in lieu of a better explanation, thought that it was caused by some unknown agent in the atmosphere.

The parasitic cause of the condition was first discovered in 1880 by Laveran, who found the *P. malariæ* in the blood of a patient suffering from malaria.

Seven years later, Golgi, Canalis, Marchiafava, Celli,

and others distinguished the parasites of benign tertian, quartan, and malignant tertian malarial fever.

Ross has the credit for the discovery of the developmental cycle of the parasite in the mosquito, while Grassi, Bignami, and Bastianelli followed out and described this development in connection with the human parasite.

Manson, Castellani, and many others have done excellent work on the subject.

CLIMATOLOGY.—Malaria occurs in its severest forms in tropical and sub-tropical countries. In Macedonia and West Africa it is probably at its very worst, due to the fact that in these parts the *P. falciparum*, the most virulent of all types of malaria parasite, is extremely common. The natives are chronic carriers of the gametocytes, and the anopheline mosquitoes which inhabit the swamps—the chief geographical feature of these regions—suck blood from the infected persons and spread the disease with great rapidity and certainty.

The disease in more temperate and less moist climates is not so severe. In India it seldom attains the degree of malignancy which it reaches in the Salonika area. In other parts of Asia, Africa and Europe and in America and Australia it is widespread.

There have always been anopheline mosquitoes in the low-lying swampy districts of the Old Country, and the return of large numbers of soldiers with the malaria parasites in their blood has caused an unprecedented outbreak of the disease in England.

The malaria problem at home, and throughout the Empire, is one that will have to be dealt with in no uncertain manner if the mortality due to the war is to cease when peace is declared.

MALARIA IN MACEDONIA.—The charts, showing the daily number of cases admitted to the 28th General

1. Anopheles Mosquito.

2. Culex Mosquito.

Note the position on wall.

Hospital for the twelve months ending February 28, 1918, are very interesting. (See Appendix.)

It will be seen that the malarial season is at its height in September, October and November.

These charts, however, only roughly show the incidence of the disease because allowances must be made for the fact that the daily number of admissions to any hospital depends on the accommodation available, convoys being distributed as evenly as possible among the hospitals which have the most vacant beds. Moreover, the system followed in this hospital has been to get malaria patients up and discharge them to the convalescent depots as soon as possible. Although this makes the monthly turnover a very considerable one, it is in my opinion an extremely sound procedure, given that the men are treated with sufficient quinine after leaving hospital to prevent the disastrous effects to the internal organs which follow in the train of repeated relapses.

THE MOSQUITO.—Mosquitoes belong to the family Culicidæ. There are three sub-families sufficiently important from the point of view of transmission of the disease to require detailed description.

(1) The genus Anopheles.

(2) The genus Culex.

(3) The genus Stegomyia.

The pests which cause malaria are the anopheline mosquitoes, the *Anopheles maculipennis* especially being a carrier of the parasite.

Dengue fever has been found to be transmitted by the culicine mosquito.

The *anopheles* is small, dark in colour, with spotted wings and long palps.

The position, almost at right angles to the surface,

which it assumes when resting on a wall is most characteristic.

The female can easily be distinguished from the male by the fact that its antennæ are much less hairy. This distinction is important because the female sucks blood while the male does not. The former, therefore, is the danger and the means by which malaria is spread.

She lays her eggs in stagnant water, but more often chooses shallow pools situated in the course of slowly moving streams.

The eggs float on the surface either singly or in stellate clusters, and in less than a week the larvæ are hatched.

*The Larvæ.*—These are very small, somewhat less than a quarter of an inch long. When breathing, they lie parallel to and just below the surface of the water. This position distinguishes them from the culicine larvæ which hang nearly perpendicularly from the surface.

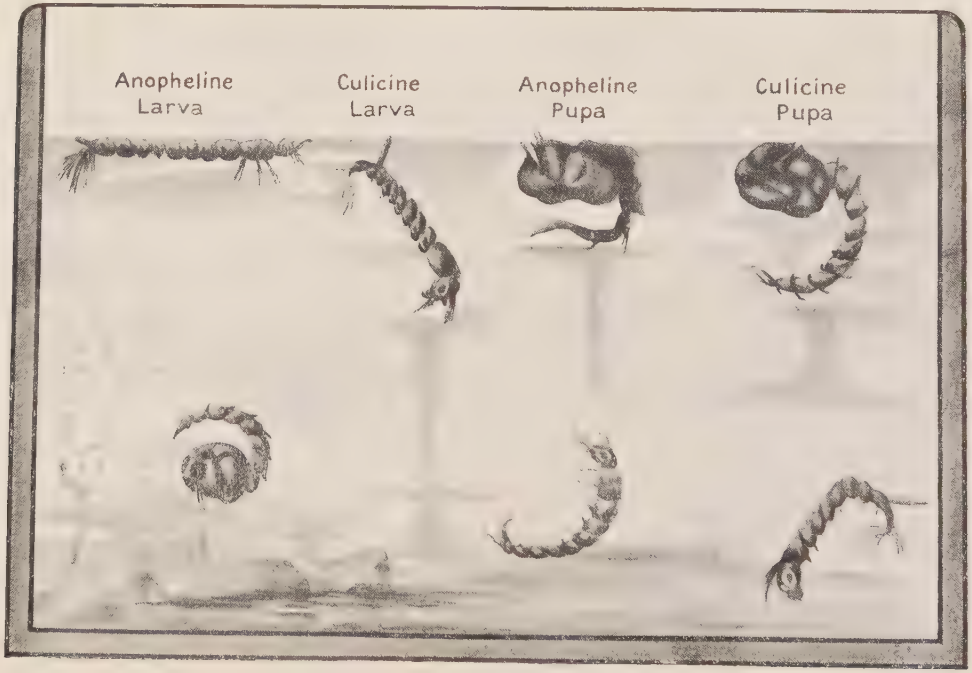
The larvæ are very active and propel themselves by sharply wriggling their bodies. They are able to remain under water without coming up to breathe for a considerable time, during which they may be seen swimming about or resting on the bottom of the pool where they obtain their nourishment.

Under suitable conditions the larvæ grow rapidly and in about ten days develop into pupæ.

The *pupa* has a more or less oval-shaped body and a curved segmented tail which it uses freely to propel itself through the water.

It generally lies under the surface, breathing by means of two respiratory tubes situated on each side of the dorsal aspect of the body, but periodically goes down to the bottom to feed.

In about a week it sheds its outer covering and the full-grown mosquito appears on the scene.




ANOPHELINE AND CULICINE LARVÆ AND PUPÆ.

Face p. 4

The *culex*, about half as large again as the anopheles, is lighter in colour, has short palps and the wings are not spotted. When resting, its body lies parallel to the surface of the wall.

The larvæ hang perpendicularly from the surface of the water with the head downwards, and breathe through a tube at the tail end.

The pupæ have their breathing tubes rather farther back, but otherwise resemble the anopheline pupæ very closely.

The *stegomyia* mosquito is nearly double the size of the culex and belongs to the same sub-family. Like the latter, it transmits dengue fever.

On account of its size and colour it is quite easily distinguished from the mosquitoes which are responsible for spreading malarial fever, and does not require any further description here.

## The Malaria Parasites.

There are three distinct varieties of malarial fever, each caused by a different species of parasite.

(1) Quartan Malaria, by the *Plasmodium malariæ*, which causes a rise of temperature every seventy-two hours due to liberation of toxins. This is followed by an apyrexial period.

(2) Benign Tertian Malaria, by the *Plasmodium vivax*, which causes fever every forty-eight hours.

(3) Malignant Tertian (or Subtertian) Malaria, due to the *Plasmodium falciparum* or *lavarania*, is characterized by a rise of temperature every thirty-six to forty-eight hours.

Quotidian malarial fever, in which a daily rise of temperature occurs, is probably a mixed infection due to two broods of tertian or three of quartan parasites, reaching maturity and bursting into the circulation on successive days.

*The Life Cycle of the Malaria Parasite in the Mosquito (Sporogony) and in Man (Schizogony).*

SPOROGONY is the sexual cycle in the female anopheline (the male is innocuous).

Microgametocytes (males) and macrogametocytes (females) are sucked with the human blood into the stomach of the mosquito. The female parasite leaves the red cell, and its nucleus divides to form with the cytoplasm the macrogametes.

Similarly, a number of mobile, thread-like bodies with chromatin dots, called microgametes, are formed by the division of the nucleus of the microgametocyte.

The micro- and macro-gametes conjugate ; their nuclei fuse and form an elongated body with a central nucleus and an accumulation of pigment at one end, called a zygote.

This becomes encysted beneath the epithelium of the stomach wall of the mosquito—the oöcyst. The latter grows, and its nucleus divides into a number of smaller nuclei, each with its own protoplasm surrounding it, called sporoblasts. The sporoblasts thus formed in turn become sporozoites by division of their nuclei. These smaller nuclei contain chromatin, and with their encircling cytoplasm project from the periphery of the cyst. The sporozoites next escape into the circulation of the mosquito, pass to its salivary glands, and later, through the hypopharyngeal canal of the proboscis into the circulation of the human being.

The sporozoites may then :—

(*a*) Develop and cause an attack of fever with rigors and sweating.

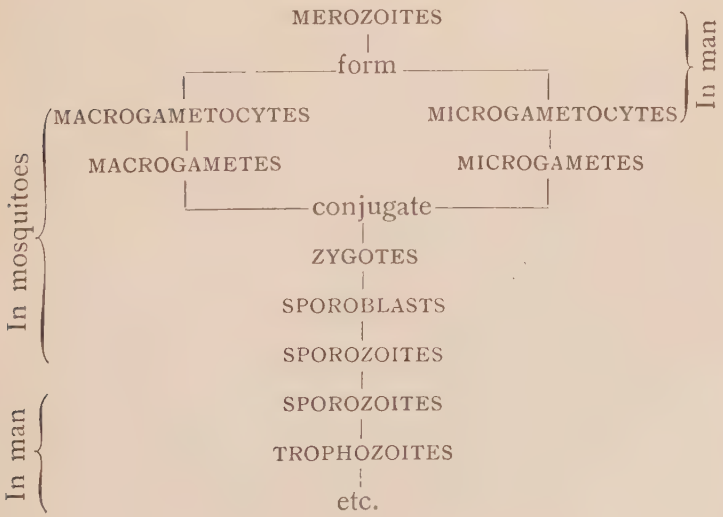
(*b*) Lie dormant in the spleen until the vitality of the patient is lowered by cold, fatigue, &c.

(*c*) Undergo destruction by the antitoxins of the blood.

Schizogony.—In man, the sporozoites, which consist of cytoplasm with a central chromatin nucleus, enter the red blood corpuscles and become trophozoites. These develop into ring forms due to the cytoplasm accumulating around the periphery ; next, dark pigmented granules appear, and the ring enlarges and becomes the adult rounded parasite called the schizont, containing numerous granules of pigment and a well-defined nucleus. The schizont undergoes segmentation, by division of its nucleus into a number of small bodies called merozoites, each consisting of cytoplasm with a small nucleus. These burst through the wall of the red cells, and with the pigment and toxins which are also liberated circulate in the blood-stream. The merozoite enters another blood-cell and becomes a trophozoite, and the cycle in man recommences.

Résumé :—

Sporogony.



SCHIZOGONY.

In mosquito ... SPOROZOITES

In man ... ...
SPOROZOITES
TROPHOZOITES
RING FORMS
SCHIZONTS (adults)
} In red corpuscles
MEROZOITES
MEROZOITES—free in circulation
TROPHOZOITES
etc.

Schizogony as it occurs in :—

(1) *Plasmodium Malariæ.*

Schizogony occupies seventy-two hours.

The trophozoite in the early stages is smaller than the benign tertian—later it increases in size.

The pigment granules are dark in colour and lie round the periphery.

The adult schizont—a later stage than the trophozoite—makes its appearance at the end of sixty hours. It is large, pigmented, and nearly fills the corpuscle ; only the outline of the latter can be seen.

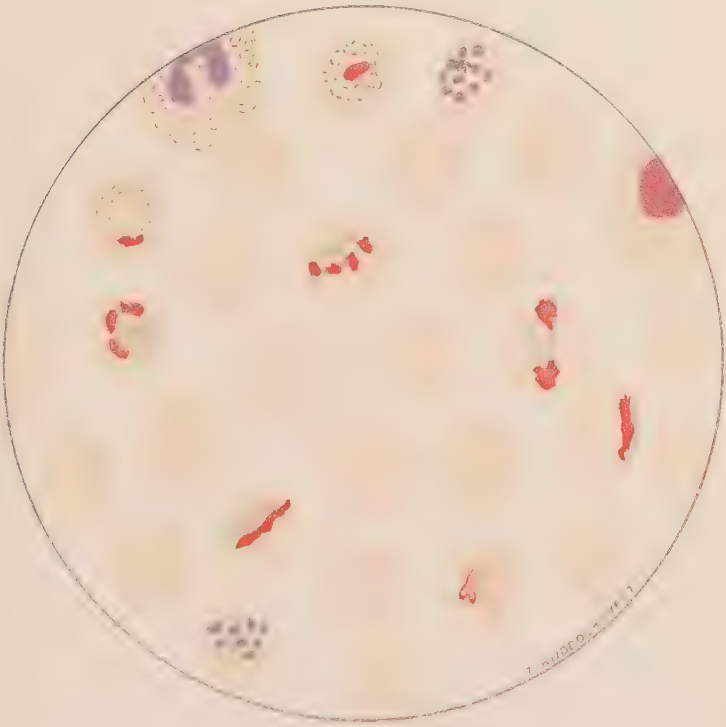
Next, the nucleus of the schizont begins to subdivide, and hæmozoin becomes collected in the centre. The result, at the end of seventy-two hours, is a central mass of hæmozoin surrounded by six to ten, usually eight, merozoites, each with its own nucleus and cytoplasm. The merozoites are then set free to circulate in the blood-stream.

# P. MALARIAE.

## Parasite of Quartan Fever.

1. Ring Form.
2. Small Band Form.
3. Larger ,, ,,
4. Segmentation of Chromatin.
5. Mature Schizont.
6. Macrogametocyte—female.
7. Microgametocyte—male.

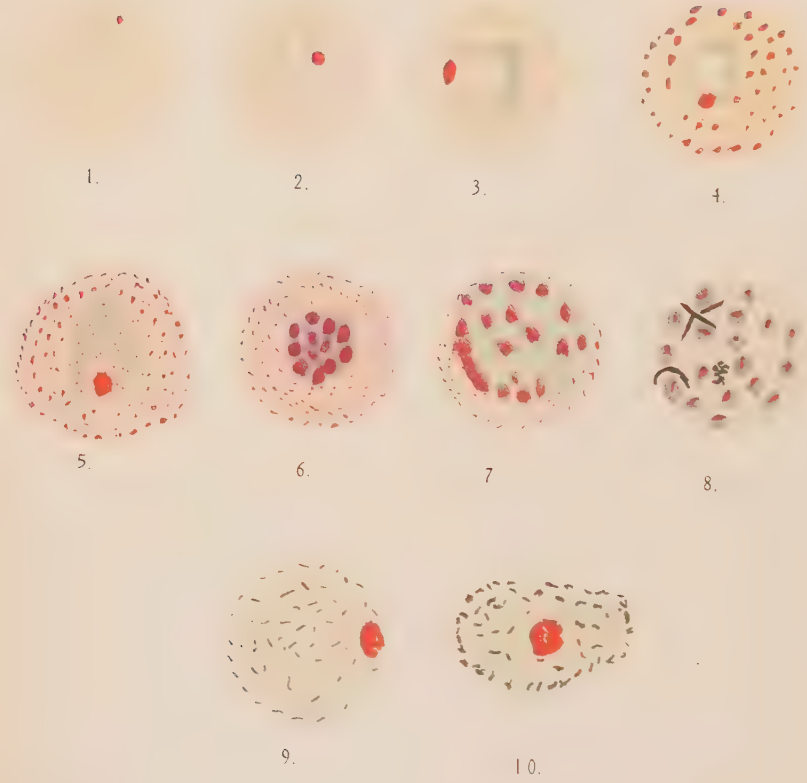
P. MALARIAE. x 1500.



Composite Field.

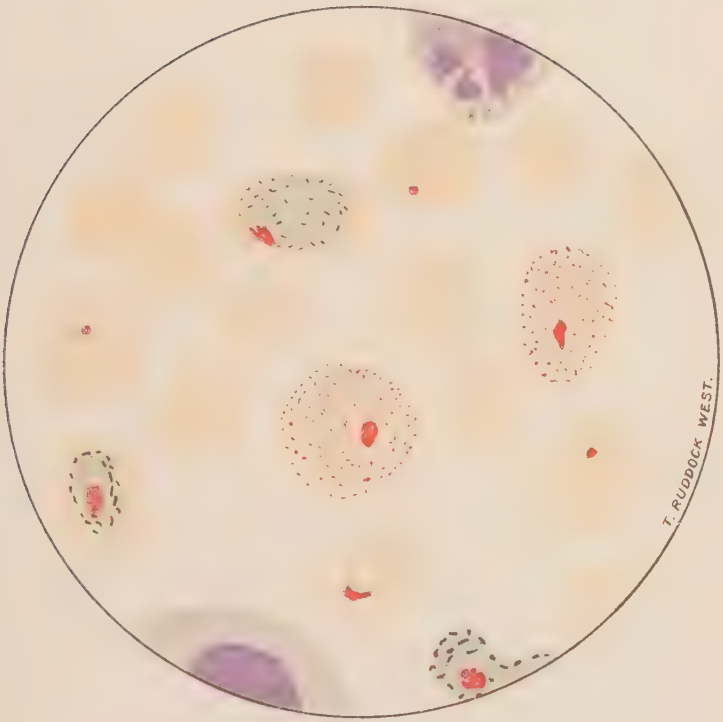
# P. VIVAX.

## Parasite of Benign Tertian Fever.



1. Small ring form.
2. Larger ring forms.
3. Larger ring forms.
4. Ring form with Schüffner's Dots.
5. Mature form
6. Schizony ,, ,, ,,
7. Later stage .. .. ..
8. Mature schizont with pigment.
9. Macrogametocyte—female.
10. Microgametocyte—male.

P. VIVAX. x 1500.

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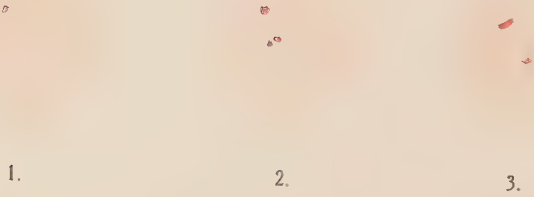
# P. FALCIPARUM.

## Parasite of Malignant Tertian, Sub-Tertian, or Aestivo-Autumnal Fever.



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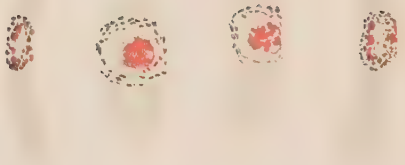


4. 5. 6. 7.

1. 2. 3. } Young Ring Forms.

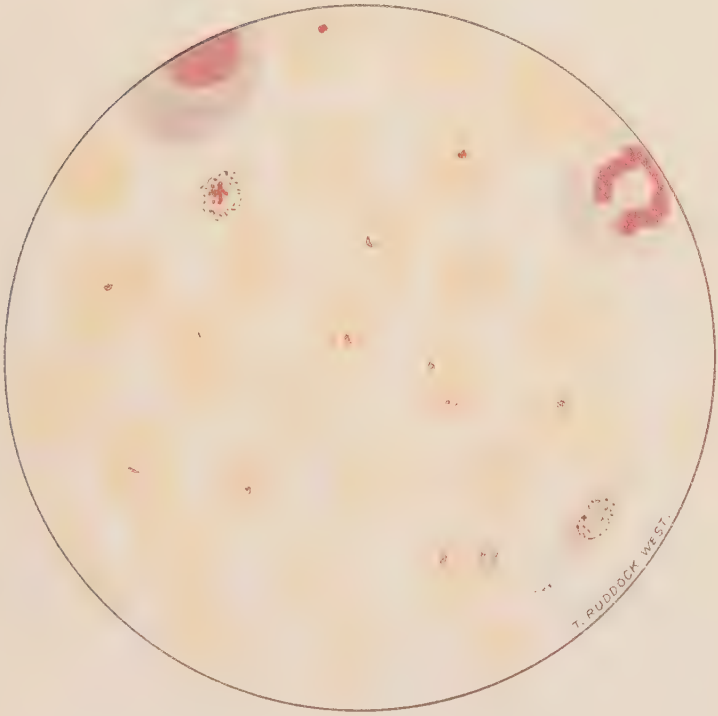
4. 7. } Microgametocytes—male.

5. Macrogametocyte—female—ovoid.

6. do. do.

} Crescents.

P. FALCIPARUM. x 1500.




Composite Field.

(2) *Plasmodium Vivax.*

Schizogony occupies forty-eight hours.

The merozoite or sporozoite, after entering the red cell, grows rapidly; the cell gets pale and degenerated through loss of hæmoglobin. Within twenty-fours hours it becomes swollen and, on staining, has a red dotted appearance—Schüffner's dots.

The parasite develops into a schizont at the end of thirty hours. It now sporulates, twelve to twenty-two merozoites being formed. These escape from the corpuscle at the end of forty-eight hours.

(3) *Plasmodium Falciparum* (*Laverania*).

The parasite of malignant tertian malaria.

The term, subtertian malarial fever, which is frequently used, is not a good one, as rises of temperature are often definitely tertian in character.

Schizogony takes from thirty-six to forty-eight hours to complete.

The young *trophozoite* is smaller than in other varieties.

The ring, which occupies only a minute part of the red cell, soon becomes oval in shape, and pigmented.

The adult *schizont* seldom appears in the peripheral circulation. It usually segments into about a dozen (eight to twenty-four) merozoites in the spleen.

The *gametocytes* are large crescents surrounded by a pale rim representing the red corpuscle.

The *macrogametocyte* (female form) is longer and thinner, and its cytoplasm lighter and less scattered than in the *microgametocyte* (male form).

Sexual Forms.—The merozoites, in all probability, assume the sexual form and develop into male and female in the course of a few days in the blood-stream.

Macrogametocyte (female), protoplasm is granular and somewhat pigmented; nucleus is small, round, rather pale and situated near the periphery.

Microgameocyte (male), protoplasm is darker in colour; nucleus is large, elongated and has more chromatin.

*Parthenogenesis.*—The gametocytes of malignant tertian may undergo regressive schizogony by parthenogenesis in the blood of the patient.

This may also occur in the quartan and benign tertian forms.

Types of Parasites.—(1) Schizont propagates the parasite in man.

(2) Microgametocyte
(3) Macrogametocyte } Propagate it in the mosquito.

The macrogametocyte in particular is difficult to destroy. It reverts to the merozoite form by division of its nucleus (parthenogenesis) when through cold, fatigue, &c., the power of resistance of the individual becomes lowered.

Relapses are often due to this cause.

Note.—(1) *The symptoms* in malaria are due to the sporulation of the parasites and the escape of toxins into the blood-stream.

(2) *The incubation period* is generally about ten days.

(3) *The apyrexial interval* is the time during which the parasite matures in the red-blood corpuscle.

(4) *The height of the temperature* and the severity of the attack depend upon the number of asexual parasites in the peripheral circulation and the amount of toxin generated.

(5) In the early stages it is almost impossible to differentiate between the various ring-forms of the parasites.

(6) Each parasite may cause the destruction of a red-blood corpuscle. It follows, therefore, that the more

parasites there are the greater the blood destruction, and the larger the amount of the toxins formed.

The toxins produced are :—

(*a*) Pyrogenetic (fever producing).

(*b*) Hæmolysin.

The corpuscles are destroyed by means of the hæmolytic toxin ; this throws more work on the liver, and causes increased bile formation. If the blood destruction is excessive, the liver cannot cope with it, and hæmoglobin appears in the urine—hæmoglobinuria.

It is possible that an antitoxin is formed by the body to neutralize the hæmolysin. This antitoxin may be reinforced by improving the general condition of the patient by good feeding, arsenic and iron tonics, &c. Quinine assists in the elimination of the poisons by the kidneys. The latter may be badly damaged by these toxins. Quinine, by destroying the parasites in the peripheral blood, prevents the formation of toxins. It is our sheet-anchor in the treatment of every type of malaria.

(7) Relapses are due to :—

(*a*) An insufficient administration of quinine ;

(*b*) The lowering of the vitality of the body ;

(*c*) The failure of the body to produce enough antitoxin.

(8) *Benign tertian parasites* cause swelling, discoloration, and degeneration of the red cells.

The trophozoite and schizont stages occur in the peripheral circulation, while the sporulating forms develop in the spleen causing enlargement and tenderness.

Malignant parasites have the opposite effect on the red corpuscles, which become smaller and darker. These parasites seldom enter the peripheral circulation ; they live and sporulate in the spleen.

The merozoite escapes into the circulation along with hæmozoin. This pigment, which may be free or ingested by the large mononuclear lymphocytes, gives rise to the dark colour of the spleen and liver found on post-mortem examination.

(9) *Anæmia* is caused by the destruction of the red cells during sporulation of the parasites.

In malarial anæmia the colour index is almost invariably low.

(10) *Leucopenia* with a relative mononuclear increase is of great assistance in the diagnosis of malaria.

(11) *Heavy Infection.*—Two or more parasites may inhabit one red cell, or a third or more corpuscles in a field may be infected.

I possess a blood-film in which at least one-third of the red corpuscles contain rings. The patient was vigorously treated with quinine and discharged to a convalescent camp three weeks after admission.

(12) *Acquired Immunity.*—In Macedonia and other malarial countries, the natives are more or less immune, having been infected since very early childhood.

Pathology of Malaria.—The following changes, mostly toxic in origin, may be found in the various organs of the body on microscopical examination.

(1) Deposition of pigment.

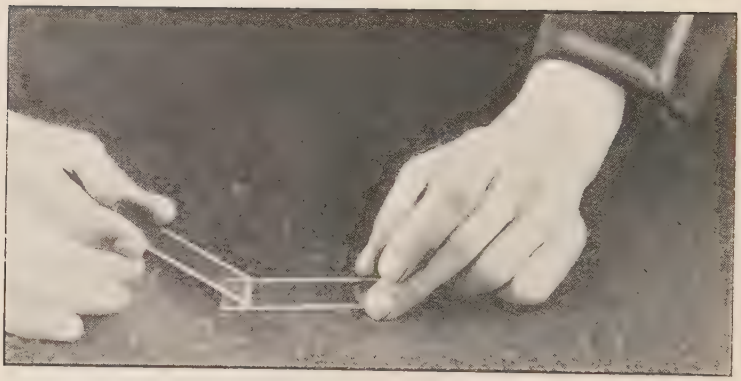
(*a*) Hæmozoin or black pigment—characteristic of malaria.

(*b*) Hæmosiderin—brown pigment.

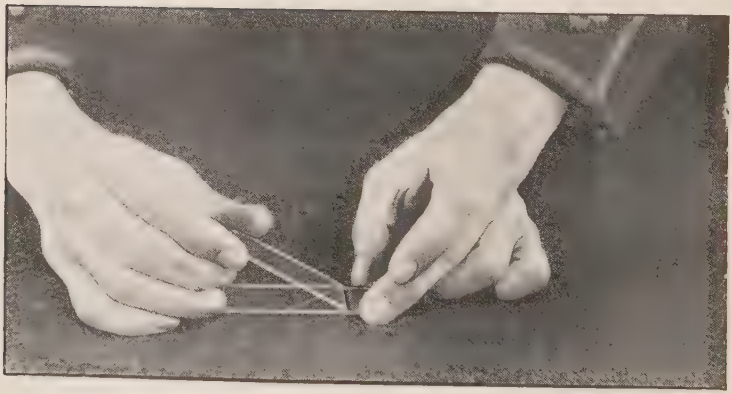
Pigment is found free in the blood-stream, in polymorphonuclear leucocytes and to a less extent in the mononuclears.

(2) Fatty degeneration of the endothelial lining cells of capillaries, arteries, and veins.

(3) Hæmorrhages.



Preparation of a blood-film. The start.



Preparation of a blood-film. The finish.

(4) Areas of necrosis.

(5) Inflammatory changes—the perivascular lymphatics being filled with lymphocytes.

Detailed description :—

Brain (see Cerebral Malaria, p. 31).

Heart.—Fatty degeneration and myocarditis.

Spleen.—There may be perisplenitis, numerous crescents may be found in malignant cases. Malpighian bodies and pulp show fatty degeneration. Pigment is found free, and in the cells of the spleen, especially in the polymorphonuclear leucocytes and the endothelial lining cells.

Liver.—Fatty degeneration of the endothelial cells most marked in the centre of the lobules round the hepatic vein. Free pigment may be present, and also pigment in the endothelial lining cells of the capillaries and in the liver cells. Crescents and a few merozoites may be seen.

Kidney.—Fatty degeneration and cloudy swelling may be present. Pigment and malaria parasites are sometimes in evidence. Very little change, however, except in blackwater fever cases.

## Preparation and Staining of Blood-films.

*Technique.*—Clean the slide with chloroform to remove grease. Prick the finger or lobe of ear, after carefully swabbing the skin with spirit or iodine. Take up two or three small drops of blood on the slide, about a quarter of an inch from one end. Place the bottom edge of another slide immediately in front of the drops, and draw it backwards until the blood has run along the margin of contact. The angle between the two slides should be about 45°. Push the upper slide slowly forward until the blood spreads in a thin film over the greater part of the surface of the lower one. Dry in air without

heating. If a thicker film is required increase the angle between the slides; if a thinner one is wanted, diminish the angle.

*Methods of Staining.*—The most widely used stain for malaria parasites is Leïshman's modification of Romanowsky's stain. It is a combination of methylene blue and eosin. The best results are obtained by staining with a few drops of Leishman's stain for half a minute; then add double the quantity of distilled water, mix well and allow the diluted stain to remain on for a further ten minutes. Wash in tap water, dry with blotting-paper, and examine with a $\frac{1}{12}$-in. oil immersion lens and a six-magnification eyepiece.

Giemsa's stain may be used instead of Leishman's. With this, it is necessary first to fix the film in absolute alcohol for ten minutes, and then dry with filter paper.

Dilute the stain by adding one part to seven parts of water, pour on to the slide and let it stand for from one to two hours. Wash and dry in the usual way.

Wright's modification of Leishman's or Jenner's stain may also be used.

*Points of Importance.*—(1) Unless the slide is absolutely free from grease the film will be useless.

(2) In staining films, the times given above should be strictly adhered to. Under-stained and over-stained films are practically worthless.

(3) A negative film does not necessarily mean that the parasite is not in the blood—try another slide. Before returning a slide as negative, examine for at least twenty minutes.

(4) The parasite of benign tertian and quartan are generally discovered within twenty-four hours after the temperature has reached its highest point. In malignant tertian, the parasites should be looked for just before the

temperature rises; crescents, however, are more often found during the apyrexial interval.

(5) Stains should as far as possible be freshly prepared. In Salonika, during the Summer of 1917—due probably to the excessive heat and the damp atmosphere—the stains decomposed and for a time almost every film examined was returned as negative.

## CHAPTER II.

### PROPHYLAXIS.

(1) QUININE PROPHYLAXIS.—I merely mention this in order to advise persons living in malarial districts not to adopt this so-called preventative measure. It has been extensively tried in the Salonika area and has proved to be an absolute failure. I made a point of finding out whether patients admitted to this hospital suffering from primary malaria during the summer and autumn of 1917 had received the routine 15 grains bi-weekly, and in nearly every case the answer was in the affirmative.

Major Castellani told me in December, 1916, that in his opinion anything less than 10 grains a day was useless. I go further, and suggest that double that amount would not be effective. Even if it were, it appears to me that to submit healthy individuals to treatment such as this for long periods makes the prevention worse than the cure. It is much more sound to adopt reasonable measures, and if after that the disease is contracted, then is the time to use quinine freely.

(2) MOSQUITO-PROOF HOUSES AND HUTS.—Where possible these should always be used. It is not advisable however to go to extremes. I have known men waste both time and material in a laudable but fatuous endeavour to prevent malarial infection by fitting mosquito-proof doors to marquees. This is very human, but in utility ranks with prophylactic quinine.

(3) MOSQUITO NETS.—Apart from a direct attack on

CAMP BED,

with sand-fly and mosquito-proof curtain in position, on the verandah of a Turkish house three kilomètres from the firing line.

the mosquito through the medium of drainage, this is the soundest way to deal with the problem.

Every man should sleep under a mosquito net and take the utmost care to prevent himself from being bitten. It is the duty of everyone to observe these precautions, not only for their own sakes but in the interest of all of us who will have to pay in rates and taxes for their sins of omission.

(4) Other Common-sense Precautions. — It is hardly wise for men living in mosquito-proof huts and sleeping under nets to sit outside after sundown and allow the mosquito to bite them, merely because it is cooler and more pleasant than inside.

Open-air theatres in the summer months are one of the malaria parasites' most valuable assets. Moreover, mosquito-proof doors which are kept carefully closed during the day are very apt to be flung widely open at night. These things have happened and will probably occur again, but they are hardly justifiable either from a selfish, a patriotic, or a common-sense standpoint.

(5) Malarial Drainage. — Extensive schemes for draining the Macedonian swamps have been undertaken during the last few years and the results have been most satisfactory.

It is a *sine qua non* that experience, and experience only, justifies a man in venturing opinions on any given subject. In dealing with the drainage of swamps and stagnant water generally, I propose to give as briefly as possible one of my own experiences in this matter.

Early in the spring of 1917, I was second in command of a stationary hospital attached to the Serbian Army and situated within a stone's throw of a village about 100 miles from Salonika. The inhabitants were all suffering from chronic malaria. Children with sallow

complexions and enlarged spleens were the rule. The prospect of living in the place was not exhilarating.

There were about 300 English sisters, medical officers and orderlies attached to surrounding units, besides a fairly large Serbian, French and Russian community. It was quite evident that something had to be done. So, after careful investigation, I approached my commanding officer and suggested that I might be allowed to tackle the problem of draining the stagnant water and surface springs situated below the village into a lake about two kilometres away.

Meeting with little or no encouragement because of the assumed possibility of the water finding its way up the proposed canal from the lake to the village instead of in the opposite direction, I called a meeting of the Macedonian mayor of the town and the Serbian and French commandants. After putting the whole matter before them, I guaranteed that if they would supply me with the labour and implements, I would bring the scheme to a successful conclusion.

My suggestion met with unqualified approval, especially from the mayor—a very intelligent person—who informed me that malaria had always been the curse of the place, and that if I would carry out what I claimed to be able to do, I should be conferring a lasting benefit on the community.

With the assistance of Captain Popovitch, the Serbian disciplinarian officer of a neighbouring hospital, I proceeded to take the levels of the ground between the village and the lake. The instruments we used were a four-metre board, a spirit-level and the handle of a long spade. This method, although crude, served the purpose, and we found we had a fall of about 20 feet from the swamps to the lake. The levels were checked two

months later by a major belonging to the Serbian Topographical Staff, and the fall, according to his calculations, was just over 16 feet.

Having satisfied ourselves that the levels were right, we started to dig the canal with the aid of twenty Bulgar prisoners lent by the Serbian commandant, ten Turks supplied by the French, and eight Macedonian civilian labourers—the gift of the mayor. The spades and picks were supplied partly by the Serbians and partly by the civilians of the town.

For six weeks the work progressed apace until the Serbian and French labourers were sent away to work at road-making, and we were left with half a dozen Macedonians who demanded pay at the rate of three francs a day and their food. Failing this, they threatened to go on strike. In desperation, I got a week's leave and went to Salonika where I interviewed the Serbian and French headquarters. On returning, I had eighty men at my disposal, and in a month's time all but finished the work. Unfortunately at this stage I was removed from my unit and ordered to report immediately for duty at the base. This gave me exactly seven hours in which to drive the canal through the most swampy and worst part of the ground—a distance of 200 metres.

Collecting every available man, I proceeded to the task of finishing what I had set out to do. I reduced slave-driving to a fine art. There was no time to rest, and we were forced to work up to our thighs in water, but the men appeared to realize that a special effort on their part was necessary, and I had the satisfaction before 8 o'clock that night of seeing the water streaming steadily from the uppermost part of the swamps to the lake below.

Of course the work was not complete; a good deal had still to be done, but I handed it over to my colleague,

Captain Popovitch, who finally completed it about three weeks later. It has since been taken over by the French Malarial Commission, who are keeping it in repair.

The canal, which is one and a quarter miles long and at its deepest part ten feet wide and seven feet deep, drained millions of gallons of water from a waterlogged area about a quarter of a mile square. This reclaimed ground is now under cultivation, having been converted into vegetable and flower gardens by the people of the town.

The water from the surface springs, which is not used for irrigation purposes, is allowed to flow down the canal and loses itself in Lake Petrescoe.

It is satisfactory to know that very few cases of malaria occurred in the place last season, and these can be traced to a few scattered pools which were unfortunately not filled in after I left.

*Filling In.*—Places which cannot be drained should be filled in with earth.

*Paraffin Spraying.*—If it is impossible to adopt other methods, paraffin should be sprayed over the pools. One pint of paraffin to about 200 square feet of surface is usually sufficient.

In places where large areas of water require treatment, a mixture of paraffin one part and green tar oil one part may be used. This mixture has the advantage of being cheap and is quite efficacious.

It is necessary before oiling to remove any vegetation covering the surface or growing in the water, and to spray in the direction the wind is blowing.

A thin layer of paraffin spreads over the surface and when the larvæ come up for air their breathing tubes are unable to penetrate the film and they become asphyxiated and sink to the bottom. It has also been found that the paraffin poisons the larvæ.

Diagram of the Canal
between the village of Sorovitch and Lake Petrescoe,
Macedonia.

Face p. 20

Tanks, cisterns, fire buckets and any receptacle containing fresh or stagnant water should be treated with paraffin in a similar manner unless it is possible to cover them adequately enough to prevent mosquitoes getting in and breeding there.

In slowly running water, the "oil drip" method should be used. This is perfectly simple. An ordinary petroleum tin with a nail driven through the bottom and a piece of waste inserted between, to regulate the flow, is all that is required. The tin is filled with cheap paraffin and placed on a raised platform at the head of the stream. The rate of flow of the oil should be about three drops per second.

*Creosol.*—This has a more deadly effect on the larvæ and pupæ than paraffin. An extremely weak solution of creosol rapidly kills the young of the mosquito, and it should be used wherever possible. Creosol drip : I have never seen this tried, but suggest it as a method for dealing with larvæ in small streams near camps, &c.

*Drainage* is by far the best method of dealing with the malaria problem. It is very much easier to prevent the disease than to cure it.

This should always be borne in mind and put into practice on every conceivable occasion.

*Anti-malaria Precautions on the Struma.*—I have nothing but praise for the way the authorities are endeavouring to prevent malaria at the Front. The Struma Valley abounds with mosquitoes, and the problem of dealing with malaria in the summer and autumn is an extraordinarily difficult one.

The precautions taken are as follows :—

In the hot months all troops except those necessary to hold the line are withdrawn to summer camps on the hills where there are comparatively few mosquitoes.

The whole area occupied by British troops is divided into districts with a medical officer acting as anti-malaria officer in each.

*Anti-malaria officers* supervise all anti-malaria work, advise commanding officers and regimental medical officers in regard to preventative measures in and around their camps, and make periodical inspections.

*Anti-malaria Squads.*—In the base and lines of communication area, and in each corps area, a number of squads consisting of twenty-six men each are available for anti-malaria work. Each battalion as well has a squad of twenty-one men of all ranks, 3 per cent. of the strength.

The latter are a permanent fatigue, that is, they cannot be changed and are told off to work under the regimental medical officer.

The duties of the anti-malaria squads include the treatment of breeding places in and around the camp, and searching for and killing mosquitoes in huts, nets, tents, &c. I think, however, a better method of dealing with the adult mosquito is a fatigue of every available man in the battalion. These should be employed for twenty minutes, morning and evening, straffing mosquitoes. The men should be responsible for seeing that there are no mosquitoes under their bivy nets, and if on inspection by an officer a mosquito is found inside the net both men in the bivy should be punished.

*Bivouac Nets.*—All officers and men who are not provided with hospital pattern or other nets, must sleep under a bivouac-pattern net. Each net when pitched covers a space ten feet broad, by seven feet long, and the centre poles are three feet above the ground. The net is covered by a waterproof sheet, ten feet wide by five feet long, for protection against the weather. The lower

border of the net is kept in position by pockets filled with sand. It is advisable to excavate the site to a depth of one and a half to three feet, before pitching the bivy. This gives more room for the two men who occupy it, and does away with the possibility of their being bitten through the net, should it sag and come into contact with some part of their anatomy.

All ranks are carefully instructed in the proper method of using the net. These nets must be in position by sundown at latest, and if there are no mosquito-proof shelters available the troops must be under the nets during the time the mosquitoes are biting.

Mosquitoes only bite when it is hot. In the winter they do not suck blood at all, but on the Struma they commence as early as February. On a warm sunny day at this time of the year, they will bite at noon. As the summer advances their period of activity becomes later and later. By May they are found to be biting in the early morning, and evening only, while at the height of the hot season, July and August, they are busy all night. This activity gradually decreases through the autumn, until the winter arrives and they become innocuous, and so the cycle goes on.

*Inspection of Nets.*—Nets are inspected daily by the platoon commanders, company commanders, or other officers. All holes or tears are at once repaired, and defects in pitching remedied. Nightly inspections are made after the troops have turned in.

*Surprise Inspections.*—Generals, commanding officers, medical officers, and officers of all ranks make surprise inspections at various times, and if the regulations laid down in regard to the necessary precautions to be taken are not strictly complied with, the individuals responsible are severely dealt with.

Mosquito-proof huts have been erected for the men to sit in while the mosquitoes are biting; where these are not available, the men not on duty must retire to their bivouacs and remain under their nets.

*Precautions against Fire.*—The nets are rendered non-inflammable by soaking them in a solution of ammonium chloride (8 ounces), in water (1 gallon).

*Head Nets and Gloves.*—Men on duty at night are provided with head nets and gloves. These must be worn on all occasions except on patrols, raids, and larger operations where the nature of the duty renders the use of these precautions impossible. Men paraded for duty with head nets and gloves are inspected by an officer to see that they are intact and properly adjusted.

*Whitewashing* of the interior of dugouts and huts. This is done as a routine, to enable the adult mosquito to be more easily seen and destroyed.

*Ointment.*—This is issued to the troops, but is of little use in preventing mosquitoes from biting.

*Destruction of Larvæ.*—(1) All small streams in dongas, pools, and other breeding places within 440 yards of a camp are dealt with by the unit anti-malaria squad. The streams are canalized to prevent water stagnating in small pools along their course, and the banks are lined with stone to prevent damage to the canals. All parts where anti-malaria work has been done are put out of bounds to all troops and animals, thereby preventing contamination of the water, if it is being conserved lower down for drinking purposes, and also damage to the canal. Small collections of water are drained, emptied, or covered with earth.

Large pools are drained, pumped dry, or filled in. Permanent pools or streams are treated by removing the weeds and oiling with paraffin one part, green oil one part, thrice weekly.

*Bush and undergrowth* within 440 yards of the camp has to be cut down and burned, as mosquitoes take refuge in such scrub during the day. It will be seen that the precautions taken to prevent malaria are pretty comprehensive. The one criticism I have to make in relation to the anti-malaria work on the Macedonian front is that a great deal of the work could and should be done in the cold months, and not left until the late spring.

Unfortunately, most of the troops in the country have already contracted malaria, and if the treatment of the disease was conducted on the same rational and thorough lines as the prophylaxis there could be no complaint at all.

## CHAPTER III.

### CLINICAL FEATURES OF ACUTE MALARIA.

THE attack usually occurs in the afternoon. It may be divided into three stages :—

(*a*) The cold stage ;

(*b*) The hot stage ;

(*c*) The sweating stage.

These stages pass insensibly into one another, are often preceded by prodromata, and are generally followed by an apyrexial interval.

(1) BENIGN TERTIAN, due to the *Plasmodium vivax*, is the most common type of malarial fever met with.

*Prodromata.*—Headache, pains in back and legs, lassitude and loss of appetite.

*The Attack.*—Severe headache, pains all over body, giddiness, nausea and often vomiting with or without a rise of temperature. The tongue is coated with thick fur.

*The Cold Stage* is characterized by a steady rise of temperature, a feeling of coldness, a chattering of teeth, and shivering which may be so violent as to shake the bed. This stage lasts for upwards of half an hour. The patient covers himself over with blankets, overcoat, or any other available wrap ; these he throws off again in the next stage.

*The Hot Stage.*—The temperature may be 105° F. or over. The skin is flushed and dry and may be slightly jaundiced. The conjunctivæ are often icteric and injected.

Heart.—A mitral systolic murmur and a reduplicated second pulmonary sound are usually heard.

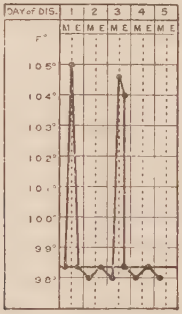
The pulse is full and bounding and its rate is increased.

Lungs.—A few scattered râles are usually present.

Spleen.—Enlarged and tender due to congestion.

Herpes labialis is common.

This stage lasts from two to eight hours.




To illustrate description of Typical Benign Tertian.

*The Sweating Stage.*—This succeeds the hot stage and may continue for four or five hours. Profuse sweating breaks out, the temperature rapidly returns to normal, the pulse rate diminishes and the patient becomes quite comfortable and falls asleep.

*The Apyrexial Interval*—For the next thirty-six hours or so the temperature remains normal or subnormal and the patient feels fit to get up. The next attack follows a similar course but can be prevented by giving sufficient quinine to destroy the parasites immediately sporulation occurs. The actual sporulation takes place in the spleen and other internal organs, but the parasites live in the peripheral circulation. Without treatment, frequent relapses, with considerable blood destruction, result.

(2) QUARTAN FEVER.—Caused by the *P. malariæ* is comparatively rare.

*Prodromata*—Headache, general malaise, nausea or vomiting, and generally a thickly furred tongue. The patient complains of feeling weak, ill, and unable to go about his ordinary work.

*The Cold Stage* is similar to that in benign tertian malaria. The rigor may be more severe, and the headache, pains in back and limbs are very intense. Vomiting is a frequent symptom and diarrhœa sometimes occurs. The temperature gradually rises, reaching its highest point in the next stage.

*The Hot Stage*—The skin is hot and dry. Conjunctivæ icteric and slightly injected.

To illustrate description of Typical Simple Quartan.

Heart.—A mitral systolic bruit and a reduplicated second pulmonary are quite common.

The pulse is full and rapid.

Spleen enlarged and tender.

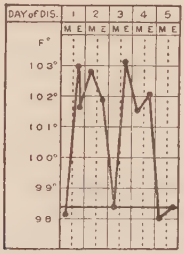
Herpes may be present.

*The Sweating Stage*, in which the pulse and temperature return to normal, is succeeded by an apyrexial period during which the patient, although weak, feels sufficiently well to move about and do light work.

The acute attack, which closely resembles the benign tertian one, lasts for nearly twelve hours. It can only be

distinguished from the latter by the different characters in the parasites and by the fact that the apyrexial interval continues for about eighteen hours longer. If properly and promptly treated with quinine the parasites disappear from the blood, a second attack is prevented, and unless a differential diagnosis has already been made it is impossible to distinguish between the two types.

(3) MALIGNANT TERTIAN MALARIA is due to the *P. laverania* or *falciparum*. This parasite sporulates and passes its life almost entirely in the spleen and internal organs. The crescents, which are very resistant to quinine, are usually the only form found in the peripheral blood. For this reason, this type of the fever is very difficult to cure and is more dangerous to life than other forms.




To illustrate description of Typical Malignant Tertian.

*Prodromata.*—As in benign tertian malaria, the actual attack is preceded by headache, pains in back and limbs loss of appetite and sometimes nausea and vomiting.

*The Cold Stage.*—The rigor may be severe, but slight shivers may be the only symptom.

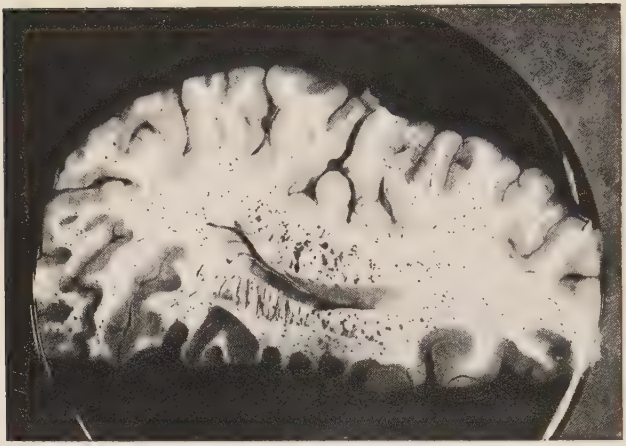
*The Hot Stage.*—The headache and the pains in back, arms and legs may be very intense. The tongue is coated with a yellowish white fur. Nausea and vomiting are common features. Diarrhœa, with a little blood and mucus in the stool, may occur. This clears up in a few

days if treated promptly with quinine and sodium sulphate. Although the Shiga and Flexner bacilli and the amœba are seldom found, the condition is probably an early stage of true dysentery. The skin is flushed and slightly jaundiced, while the conjunctivæ have an icteric tinge and are injected. The spleen is palpable and tender, and the liver may be enlarged and tender as well. The temperature is deceptive and there is often little or no elevation. On the other hand, a sharp rise to 105° F. or 106° F. may take place. Instead of dropping rapidly again as is the case in other types of the fever, it usually remains up for twenty-four hours with only a slight fluctuation of about one degree. A moderate temperature is, however, the rule. The apyrexial interval depends upon the length of the attack and may be very short—twelve hours or even less.

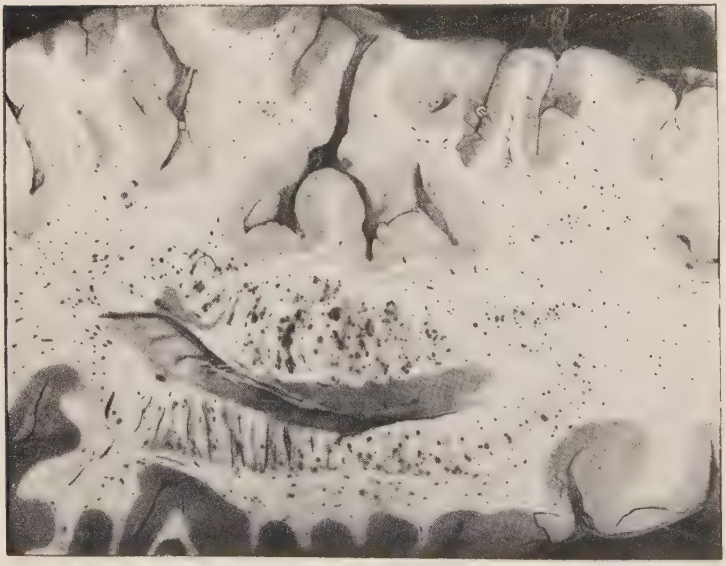
The second attack may be aborted or prevented altogether by the administration of large doses of quinine intramuscularly or per rectum. The oral route should only be used if the bowels have been freely moved and the tongue is clean and moist. This is a very important point in the prevention of malarial recurrences. A patient who is constipated and has a thickly furred or dry tongue does not appear to absorb quinine given by the mouth. At any rate, experience shows that unless the bowels are carefully regulated the results obtained from quinine by the mouth are most disappointing.

### Pernicious Manifestations of Malarial Fever.

These are generally caused by the malignant tertian parasite, but I have on rare occasion found the *P. vivax* in the blood of patients suffering from one or other of these pernicious fevers. It is possible that these cases



Cut section of brain in cerebral malaria, showing petechial hæmorrhages.



Cut section of brain in cerebral malaria, showing petechial hæmorrhages. The surface of the brain seen here is the exact size of the specimen photographed.

Face p. 31.

may have been instances of a double infection—by both the *P. vivax* and *P. falciparum*. The following are the forms most commonly met with :—

(1) Cerebral Malaria is an acute general toxæmia chiefly affecting the brain. If untreated with quinine it rapidly causes death.

*Pathology.*—On post-mortem examination numerous petechial hæmorrhages are found scattered over the surface of the cut sections. These hæmorrhages are only found in the white matter and in the internal capsule. I have been unable to find the slightest trace of them in the grey matter. The white matter has a poor blood supply, and the capillary walls of the internal capsule and white matter are extremely delicate. In the grey matter, on the other hand, the blood supply is better and the capillary walls stronger. The petechial hæmorrhages are due to a degeneration of the endothelial lining cells of the capillaries and may cause necrotic changes. Necrotic areas, like the hæmorrhages, are always found in the white matter, and not in the grey matter. Degenerative changes are found in the endothelial cells of the minute vessels of the grey matter, the meninges, nerve cells and fibres, but do not result in hæmorrhages and necrosis in these parts. It should also be noted that although crescents and merozoites are found in all the vessels of the brain, the former are chiefly located in the white, while the latter are more numerous in the grey matter.

Castellani and other authorities hold that the hæmorrhages and necrotic changes are caused by red blood corpuscles, altered by the parasite, adhering to the walls of the capillaries, and that these, together with swollen endothelial cells containing pigment, and pigment free in the blood-stream, form thrombi. This is possible,

although the red cells do not appear to be altered in any way.

I am of opinion, however, that the condition is not due to an accumulation in the minute vessels and substance of the brain, but to the fatty degeneration mentioned above causing rupture of the delicate capillary walls, and consequent tiny hæmorrhages and necrosis.

*Clinical Aspect of Cerebral Malaria.*—The group of symptoms due to cerebral toxæmia are extraordinarily varied.

In Macedonia, medical officers of experience are never surprised at finding obscure nervous symptoms in patients suffering from malaria. They treat them vigorously with quinine and if the drug is given in sufficient quantities and by the correct methods the condition soon clears up.

*Symptoms.*—Drowsiness, semi-coma and coma are the stages through which cerebral cases pass. Sometimes, however, the early stages are hardly appreciable, and sudden coma and death may result if any time is lost in treating the patient. Headache is constant but not so severe as in cerebrospinal meningitis. The blood-film is of assistance in diagnosis—if the parasite is found or there is a mononuclear increase. Polymorphonuclear leucocytes indicate sepsis and the reason for their presence should be immediately looked for.

I strongly advise the use of lumbar puncture as a routine in all cases with cerebral symptoms. The operation which is described later is quite easy to perform, and in the event of a failure to find a cause in the chest or abdomen for the polymorphonuclear increase, the cerebrospinal fluid should at once be examined.

Delirium, with or without contraction of the limbs, aphasia, ataxia and the other signs of disturbance of the central nervous system, are apt to occur.

A perusal of the case-sheets detailed in the next chapters will, however, go further towards initiating the embryonic malarial expert into the mysteries of cerebro-spinal malaria than any written description.

(2) ALGID MALARIA is characterized by severe rigors without any rise of temperature. The pulse is fast and thready and the respirations rapid. The patient is cyanosed and extremely collapsed, and unless, as in nearly all the other cases of pernicious malaria, early treatment is undertaken, death will speedily result.

*Malarial Amblyopia.*—Blindness may follow an attack of one of the pernicious forms of malaria. It may affect one or both eyes and is due to hæmorrhages from the minute retinal vessels. The pupils are normal and react to light, and the condition, if treated with quinine, soon passes off. Permanent blindness is rare, but may occur. Amaurosis due to malaria must be carefully distinguished from that caused by quinine, because in the latter case, if the drug is persisted with, total and permanent blindness will result.

*Quinine Amblyopia.*—In *quinine amblyopia* (see chapter on Blackwater Fever) the pupils are dilated, but slowly react to strong light. One large dose of quinine may be disastrous and cause complete loss of eyesight. The case of a hospital orderly who swallowed half an ounce of quinine to show a recalcitrant patient how it should be done, is an instance of this. Comparatively small doses may cause amblyopia if the individual has an idiosyncrasy towards quinine. This is, however, so rare that it only requires mention. Dosage with 60 to 120 grains spread over a period of from twelve to twenty-four hours is quite safe, but in blackwater fever it may cause transient blindness on account of the drug not being excreted rapidly enough by the kidneys. In this disease,

the maximum dose in twenty-four hours should not exceed 60 grains—if there is any diminution in the amount of urine passed by the patient. As soon as the daily quantity becomes normal again, a larger amount of quinine may be given. The sight returns on stopping the quinine administration, and there appear to be no bad after-effects. On ophthalmoscopic examination, the colour of the optic discs is found to be rather paler than normal. The retinal vessels show some contraction.

(3) Latent Malaria.—Parasites can often be demonstrated in the blood of patients who show no clinical symptoms of any kind. Many observers, besides myself, have noted this fact, which is of the greatest importance, because some authorities contend that it is possible to treat malaria successfully by waiting for the attack of fever to occur and then giving large doses of quinine. Unless the existence of latent malaria is denied altogether, this method is both unsound and dangerous inasmuch that it allows the toxins during this apyrexial period free scope to affect the heart, spleen and other organs of the body injuriously.

I fail to see what can be gained by waiting until the parasites have become sufficiently numerous to generate enough toxin to cause a rigor and a rise of temperature. Toxins, even in small amounts, damage the tissues, and their effect should be neutralized by quinine without delay. The best way to prove whether the opinions expressed in this book are correct is to test them.

It is unthinkable, however, that methods which have proved to be an unqualified success in the oldest and largest hospital in the Salonika Command should be a failure elsewhere.

## CHAPTER IV.

## THE TREATMENT OF MALARIA.

At a meeting of the Salonika Medical Society held at the 28th General Hospital on Wednesday, December 19, 1917, at which Major-General M. P. C. Holt, D.S.O., K.C.M.G., D.M.S., Salonika Forces, presided, and at which I read a paper on malaria, and showed cases, I made the following statement: "In my opinion no man should die of uncomplicated malaria." I repeated this statement at a meeting of the same Society held at No. 1 Convalescent Depot a fortnight later. My reason for laying down this dictum is based on facts and figures.

It is necessary here briefly to deal with these statistics as they go far towards justifying the above assertion.

*Statistics.*

| | Cases | Deaths |
|---|---|---|
| Total number of cases of malaria admitted into 28th General Hospital between November 20, 1915, and December 16, 1917 ... | 15,454 ... | 71 |
| First year: to November 20, 1916 ... ... ... ... | 6,557 ... | 55 |
| Second year: to December 16, 1917 ... ... ... ... | 8,907 ... | 16 |

My experience in this hospital only covers the second period. The total number of cases I have actually dealt with in Macedonia being about 12,000.

On October 20, 1917, I introduced what I have termed the large dose intravenous and intramuscular quinine

method of treating cerebral and other severe pernicious types of malaria.

It is impossible to deal in detail with figures so large as the above, and at the same time keep this work within reasonable limits. Therefore, I have only taken figures representing the number of admissions during the three months ending December 16, 1917—just prior to the date of the meeting of the Salonika Medical Society at this hospital—and have divided these three months into two periods, viz :—

*Period A.*—From September 17 to October 20, 1917, inclusive—that is, before the introduction of the big dose intravenous and intramuscular method of administering quinine.

*Period B.*—From October 21 to December 16, 1917—that is, after the introduction of the method.

| | Cases | Deaths |
|---|---|---|
| Total number of cases admitted during the whole period of three months ... ... ... ... | 3,945 ... | 9 |
| Number admitted during period A | 1,949 ... (roughly 2,000) | 8 |
| Number admitted during period B | 1,996 ... (roughly 2,000) | 1 |

An analysis of these figures shows that the mortality from malaria was reduced from 0·83 per cent. in 1916 to 0·18 in 1917.

Further, a comparison of the death rate in the 2,000 cases admitted during the period A (0·4 per cent.), with the mortality in the 2,000 cases admitted during the period B (0·05 per cent.), is even more startling. Moreover, the death that occurred during the latter period requires explaining and will be dealt with later.

To arrive at the true value of these figures, however, it is essential to give further details in regard to :—

(1) The number of blood-films examined and the results obtained during these periods.

(2) The number of patients placed on the "dangerously ill" list.

(3) The number of cerebral cases.

(1) Number of Blood Films examined.

| Week ending | Number of films examined | M.T. | B.T. | Quartan | Type undetermined | Parasites not found |
|---|---|---|---|---|---|---|
| Sept. 22, 1917 | 151 | 20 | 56 | 2 | 7 | 66 |
| „ 29, „ | 166 | 21 | 27 | 1 | 5 | 112 |
| Oct. 7, „ | 152 | 13 | 47 | 0 | 2 | 90 |
| „ 13, „ | 213 | 29 | 52 | 1 | 6 | 125 |
| „ 20, „ | 211 | 45 | 42 | 2 | 6 | 116 |
| „ 27, „ | 184 | 27 | 27 | 2 | 23 | 105 |
| Nov. 3, „ | 180 | 5 | 13 | 0 | 24 | 138 |
| „ 10, „ | 82 | 2 | 12 | 0 | 14 | 54 |
| „ 17, „ | 80 | 5 | 7 | 0 | 5 | 63 |
| „ 24, „ | 86 | 6 | 20 | 0 | 6 | 54 |
| Dec. 1, „ | 81 | 10 | 14 | 0 | 5 | 52 |
| „ 8, „ | 62 | 6 | 11 | 2 | 0 | 43 |
| „ 15, „ | 49 | 10 | 3 | 0 | 0 | 36 |
| | 1,697 | 119 | 331 | 10 | 103 | 1,054 |

It will be noticed that of the types definitely determined the proportions are: malignant tertian, 37 per cent.; benign tertian, 61 per cent.; quartan, 2 per cent.

The reasons for the high percentage of blood slides (1,054) in which no parasites were found are:—

(*a*) The poor quality of the stain, due to Salonika climatic conditions (moisture and heat) causing it to decompose.

(*b*) The enormous number of slides which had to be

examined every day made it impossible for the bacteriologist to give sufficient time to the examination of each slide. A slide should be searched for the parasite for at least twenty minutes before it can be definitely returned as negative. The urgent cases were of course examined with the utmost care.

(*c*) The absence of the parasite from the peripheral circulation due to quinine treatment before admission.

(2) Number of Patients on "Dangerously Ill" List.

Total number during the three months ending December 16, 1917 ... ... ... ... ... 255

| | No. | M.T. | B.T. | Primary | Recurrent | Others |
|---|---|---|---|---|---|---|
| Number of patients on D.I. list during period A ... | 162 | 101 | 1 | 8 | 16 | 36 |
| Number of patients on D.I. list during period B ... | 93 | 38 | 1 | 2 | 8 | 42 |

*Note.*—In this hospital medical officers have instructions not to put patients on the "dangerously ill" list unless it is absolutely necessary, as it is not considered fair to alarm their relatives at home without sufficient cause. It is recommended that the "seriously ill" list be used instead whenever possible.

(3) Cerebral Cases.

Number of cerebral cases in three months ending December 16, 1917 ... ... ... 20

| | Cases | | Deaths |
|---|---|---|---|
| Cerebrals in period A (2,000 cases) | 7 | ... | 4 |
| Cerebrals in period B (2,000 cases) | 13 | ... | Nil |

Here again, it will be seen that whereas in the period

before the introduction of the large dose intravenous and intramuscular method, out of seven cerebral cases 57 per cent. died. After the method was introduced, although the number of cerebral cases was nearly doubled, the mortality was nil.

The variety and the virulence of the cases I have had to deal with during the last eight months are due to the fact that the ambulance train from the Doiran front passes through this hospital, and all lying cases, too ill to be transported by ambulances to other hospitals, are sent to us.

### Methods of Administration of Quinine.

(*a*) Oral Administration.
(*b*) By Intramuscular Injections.
(*c*) By the Intravenous Route.
(*d*) Per Rectum.

Salts of Quinine.—There are three salts of quinine available for use in the treatment of malaria.

(1) *Quinine Hydrochloride*, soluble in 36 parts of water, and in 2 parts of 90 per cent. alcohol.

(2) *Quinine Sulphate*, soluble in 800 parts of water, and in 65 parts of 90 per cent. alcohol. Also 1 grain dissolves in 1 minim of dilute sulphuric acid.

(3) *Quinine Bihydrochloride* (acid quinine hydrochloride), soluble in less than one part of water. B.P. doses, 1 to 10 grains. The doses I advocate are: 10 to 40 grains for single administration, and 30 to 120 grains within a period of twelve hours in cases of emergency.

### (*a*) Oral Administration.

The drug may be administered in the form of :—

(1) Tablets.
(2) Powder.
(3) Solution.

(1) Quinine in tablet form is valueless and should never be used. I, personally, have retrieved quinine tablets from the stools of patients on a number of occasions, and these, on naked-eye inspection, appeared to be in no way different from similar tablets which had not passed through the intestinal canal. To rely on quinine tablets in the treatment of malaria is to gamble with the health of the patient, if not with his life. Quick absorption of quinine is the chief end aimed at in the treatment of every type and degree of malarial fever.

(2) Powdered quinine: this is better than the tablet form. If tablets only are available, they should be pounded and reduced to a powder, and used as such. The absorption of the powdered form is, however, uncertain. It is unpleasant to take, and the most that can be claimed for it is that it is cheap. To consider expense in dealing with a disease like malaria is false economy of the most glaring kind.

(3) Quinine in solution: wherever possible, the administration should take this form.

Quinine sulphate and bihydrochloride are the salts generally used. The former has the merit of being cheap. It should be dissolved in dilute sulphuric acid, 1 grain to 1 minim of the acid. As a rule, in dispensing the solution, more of the acid is used than is necessary. The result is that the stomach becomes upset, the quinine is not properly absorbed and the effects obtained are disappointing. *Quinine bihydrochloride, although more expensive, is very soluble in water, it is easily absorbed, and is undoubtedly the best drug for use either by the mouth, per rectum, intramuscularly or intravenously.*

(*b*) Intramuscular Injection.

(1) Disinfect the skin with iodine, and the syringe by boiling.

(2) *Quinine Solution.*—Use one part of the bihydrochloride of quinine in one part of water—carefully sterilized by boiling. Where possible, distilled water should be utilized.

*Note.*—Keep the quinine solution in a rubber-capped bottle, swab the rubber with iodine before inserting the needle, hold the bottle upside down while withdrawing the solution, and expel all air bubbles from the syringe. If an ordinary corked bottle is used, wipe the mouth carefully with 1 in 20 carbolic, or any other available antiseptic, before filling the syringe.

(3) Not less than 20 grains of the bihydrochloride of quinine (40 minims of the quinine solution) should be given.

(4) The spot selected should be about 2 in. below the middle of the crest of the ilium. The needle must be introduced perpendicularly, and if the point strikes the bone it should be withdrawn about a quarter of an inch and the quinine injected into the muscle. Care should be taken not to get any into the subcutaneous tissue, as in that case pain, stiffness, inflammation, necrosis of tissue and abscess formation may result.

(5) In repeating injections into this region endeavour not to use the same spot twice; keep at least half an inch away from a previous puncture mark, and work backwards towards the sacro-iliac articulation along a line about two inches below the crest. When a large number of injections have to be given, quinine may be introduced into the deltoid muscle at a point at about 2 inches below the acromion process. It is preferable, however, to use the rectal route rather than this site.

Instances of musculo-spiral paralysis and sciatic palsies have been reported. These are due to ignorance or carelessness on the part of the operator.

*Indications for Intramuscular Administration.* — (1) Cases of severe exhaustion, cachexia, anæmia, jaundice and apyrexial malarial infection.

(2) Blackwater fever, bilious remittent fever, &c.

(3) Cases in which the patient has a thickly furred or a dry brownish tongue. These cases will not absorb quinine given by the mouth.

(4) Cases with a temperature of over 104° F., and a dirty tongue.

(5) Patients who are vomiting.

(6) Any case which appears to be drowsy, noisy or mentally affected in any way.

Medical officers are warned specially against the fallacy of assuming that because a man on admission to hospital appears to be mentally dull, he was born that way.

In the vast majority of cases in the Salonika command, and among persons who have resided in malarial countries, the condition is due to malaria. Such patients should receive an intramuscular injection of 20 grains of quinine at once, and preparations should be made to give an intravenous injection as well at the earliest possible moment.

### (*c*) Intravenous Injection.

This is without a doubt the soundest and best method of administering quinine, in :—

(1) Cases with mental or other nervous symptoms—drowsiness, noisiness, aphasia, nervous twitchings, tendency to get out of bed, &c.

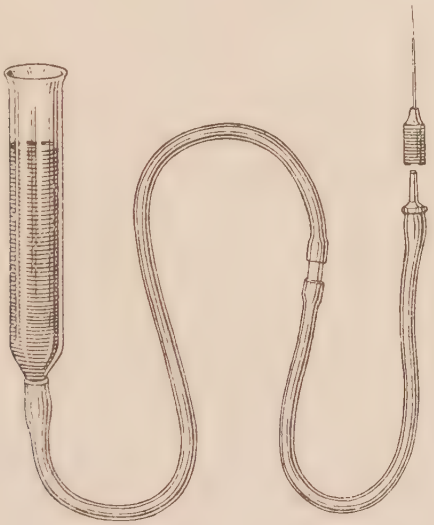
It may be laid down as an axiom that every patient suffering from malaria — clinical or otherwise — and

showing signs of a disturbance of his central nervous system, should receive an intravenous injection of quinine at the earliest possible moment.

(2) Cases of severe exhaustion, anæmia, cachexia, and jaundice, with or without a temperature.

(3) Cases of blackwater fever, bilious remittent fever, and all other types of pernicious malarial fevers.

*Intravenous Administration. Apparatus.*—(1) A glass funnel 1 in. in diameter.



Intravenous Apparatus.

(2) Three feet of rubber tubing with a glass connection inserted.

(3) Metal connection to fit a Weinstrand salvarsan needle.

(4) Weinstrand needle.

(5) A graduated measure capable of containing at least 10 ounces of fluid.

(6) A large thermometer.

(7) Some means of keeping the saline solution at the required temperature. Standing the measure in a basin of boiling water will serve the purpose.

Quinine solution—1 in 2 of the bihydrochloride of quinine in normal saline solution.

In making up the solutions, distilled water should be used if possible, but this is not essential. In 90 per cent. of the intravenous injections given by the method I advocate we have used ordinary tap water sterilized by boiling, and strained through four or five layers of gauze.

Rigors during or immediately following the injection are rare, and are of no importance.

*Technique for the administration of quinine bihydrochloride, 20 grains in 8 ounces of normal saline solution :—*

(1) Prepare 10 ounces of normal saline by adding 40 grains of sodium chloride to half a pint of distilled or sterilized water, re-boil and strain through gauze.

(2) Add 50 minims of the quinine solution (quinine bihydrochloride 25 grains) to the above.

The reason for preparing 10 ounces when only requiring 8 ounces is to make allowance for the solution left in the tube after the operation is completed, and for wastage.

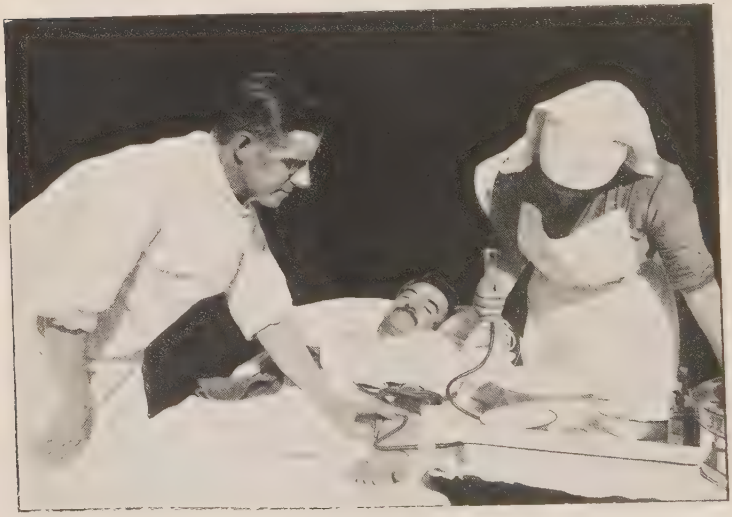
(3) The temperature of the quinine saline should be about 130° F. to allow for cooling during its course through the apparatus to the vein.

(4) See that the apparatus is sterilized, and before commencing carefully disinfect the hands.

(5) Fill the funnel and compress the tube as near the metal connection as possible.

(6) Lower the funnel, and then very slowly raise it again until the fluid trickles through the metal connection ; this will insure the expulsion of air bubbles.

Medical Officer giving an intramuscular injection. (See p. 41.)



An intravenou injection of quinine.
Note the height of the funnel above the level of the vein.

(7) Pronate and extend the patient's arm, placing a towel and a piece of waterproof sheeting beneath it to protect the bed-clothing.

(8) Disinfect the anterior aspect of the upper arm and forearm with iodine in the vicinity of the elbow-joint.

(9) Distend the veins by means of an ordinary tourniquet, a piece of rubber tubing or a bandage round the upper arm, and if the patient is conscious make him clench his hand—this helps to make the vessels more prominent.

(10) Choose a suitable vein, either the median basilic or the median cephalic.

(11) Insert the needle into the perivenous connective tissue in a direction parallel with the axis of the vein and towards the proximal end of the limb.

(12) Gently work the point, which should be sharp, into the lumen of the vessel.

(13) Immediately blood appears through the end of the needle, place a finger over it, run a few drops of the solution through the tubing, fix the metal connection to the needle without any delay, *and at once remove the tourniquet*. Before making the connection, however, it is advisable to allow a few drops of blood to escape from the needle to ensure that no clot has formed in its lumen. The solution, which will be at a temperature of about 110° F., is then run *very slowly* into the circulation. It is seldom necessary to raise the funnel more than a foot above the level of the vein.

(14) As soon as the last of the saline has disappeared into the tube, remove the needle from the vein, and seal the puncture with collodion.

*Points to remember.*—(1) Loosen the tourniquet immediately the connection has been made.

(2) Air embolism is a bogey, but all anxiety can be

removed by lowering the funnel to the full extent of the tubing beneath the level of the metal connection, and slowly raising it again before attaching it to the needle.

(3) Do not raise the funnel too high above the level of the vein—the more slowly the solution is run in the safer the operation becomes.

(4) If a swelling appears under the skin after the insertion of the needle, it means that the solution is invading the subcutaneous tissue. Remove the needle at once, and try a spot higher up, or another vein.

(5) It is often of advantage to insert the needle into the trunk of a vein at the junction of two smaller branches.

### Dangers accruing in the Administration of Quinine intravenously.

Accidents have happened while giving quinine intravenously, due to one of the following causes :—

*Danger No.* 1.—An overdose of saline causing shock, and dilatation of the right side of the heart.

Post-mortem results in the case of men who have died of cardiac failure following malaria show the walls of the heart to be thin and fatty, and the muscle atrophic.

A large quantity of saline forced through the veins into the chambers over-dilates them, and the patient collapses and dies.

*Danger No.* 2.—The injection of quinine in a too highly concentrated form. This may cause shock, and inhibit the heart's action directly or through the central nervous system, quinine being very destructive to protoplasm already diseased.

I have records of three patients who died during, or immediately after, *the injection of large quantities of saline given intravenously.*

CASE 1.—Driver S., aged 46. Service, 1 year 6 months. Diagnosis: Malaria (B.T.). Admitted on July 24, 1916. Temperature, 103° F.

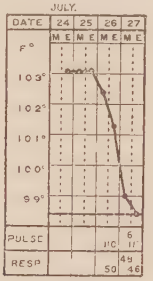
*Blood film.*—Benign tertian parasites found.

*Progress.*—July 25, 1916: Temperature, 103° F.; July 26, temperature, 102·8° F.; July 27, temperature, 99° F., pulse 116, respirations 46.

*Treatment.*—Quinine 10 grains, given intramuscularly.

July 28, 1916: Died at 5 a.m., immediately after receiving an intravenous saline, 1 pint.

*Cause of death given.*—Malaria and cardiac failure.




Case 1. Driver S.

CASE 2.—Private T., aged 42. Service, 17½ years. Diagnosis: Malaria (B.T.). Admitted August 24, 1916. Onset of present illness, August 21, 1916. Severe headache. Pain in abdomen chiefly over spleen and liver.

*On admission.*—Temperature, 105·4° F.; rigors lasting from ten to twenty minutes followed by profuse sweating; heart sounds weak; pulse irregular; jaundice marked; spleen plus and tender; vomiting.

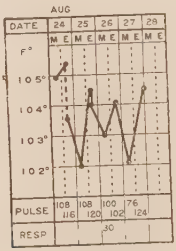
*Progress.*—August 27, 1916: Temperature varied between 102° F. and 105° F. for the four days before death. Sponged daily, but this was of little use. The persistent vomiting did not seem to be influenced by any treatment.

Intravenous quinine 10 grains in 2 pints of saline given.

Patient collapsed and died immediately after the intravenous injection.

*Cause of death given.*—Malaria.

*Comments.*—Both these deaths occurred in 1916.




Case 2. Private T.

In the first case the patient died immediately after receiving 1 pint of normal saline intravenously.

In the second case death took place immediately after an intravenous injection of 2 pints of saline with only 10 grains of quinine in it.

It is very evident that the quinine could not have been the cause of death in these cases.

Case 3.—Private W., aged 43. Service, 3 years. Diagnosis : Cerebral malaria. Admitted on August 18, 1917. In Balkans 8 months.

*On admission.*—11 a.m. : Patient admitted in a state of delirium and unable to give any account of his illness except that he has been ill for five days. Anæmia marked ; jaundice slight. His attention cannot be focused on any subject for more than a few seconds. Herpes round mouth ; tongue very dirty ; breath foul ; heart and lungs normal ; spleen much enlarged and very tender. No paralysis ; pupils react normally.

6 p.m. : Delirium gradually increasing. Jaundice becoming deeper. Pulse very rapid, thready and uncountable.

9.30 p.m. : Pulse recovered for a short time after intravenous saline and pituitrin, but soon began to fail again.

Midnight : Patient collapsed and died suddenly during the administration of 1 pint of normal saline intravenously.

*Treatment.*—

| | |
|---|---|
| 11 a.m. | Intramuscular quinine 10 grains. |
| 6 p.m. | Intravenous quinine 10 grains. |
| 7 p.m. | Intravenous saline 1 pint; pituitrin 1 cubic centimetre. |
| 9.30 p.m. | Strychnine $\frac{1}{60}$; digitalin $\frac{1}{100}$; hypod., and brandy 1 ounce by the mouth. |
| 11.45 p.m. | Intravenous saline 1 pint, during the administration of which he died. |

*Comments.*—(1) This patient was under my supervision, and died during the course of an intravenous injection of 1 pint of saline given by me.

(2) All the quinine he received from the time he was admitted to the time of his death was 20 grains.

(3) He had two large intravenous injections without quinine.

In the light of my experience since then, I am of opinion :—

(1) That I should have given him at least 100 grains of quinine during the time he was in the hospital.

(2) That in an excess of enthusiasm to give him a last fighting chance for his life, I gave him too much saline intravenously, and, moreover, allowed it to run in too rapidly.

(3) That thereby I over-dilated the heart, and caused it

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to stop in diastole, thus hastening his death by an hour or two.

(4) That had this patient been treated with the doses and by the method I now employ, he would have had as much chance of recovery as other cerebral malarias who were treated by the large dose intravenous and intramuscular method. Some of these cases were, in my opinion, in a more serious condition than this man was; yet they all recovered, and have resumed their duties.

This case is a very important one from my point of view, because on account of it I came to the conclusion that the danger in intravenous injections of quinine lies not in the quinine, but in overdoses of the saline. I resolved, therefore, that the next time it was necessary to administer quinine intravenously I would not give more than 15 ounces of saline.

The success achieved is clearly shown in the following case :—

Case 4.—Driver J., aged 26. Service, 2 years 10 months. Diagnosis: Recurrent malaria. Admitted on September 17, 1917. In Balkans, 1 year 8 months.

*Onset of present Illness.*—September 10, 1917.

*Symptoms.*—Headache, shivering, sweating, pains in back and limbs, vomiting, giddiness.

*On admission.*—Temperature 97·4° F.; pulse 72 per minute; no jaundice; tongue moist, white fur; heart and lungs normal; spleen tender and palpable; mental condition alert and normal.

9 p.m. Temperature 104° F.

*Treatment.*—Calomel 5 grains, and mag. sulph. mane.

---

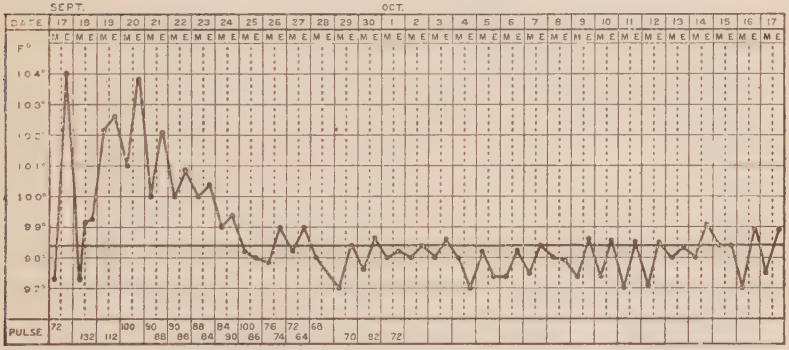
18/9/17—9 a.m. Patient much worse; semi-conscious; pulse very weak; blood and mucus in stools; no tenesmus.

*Treatment.*—Strychnine $\frac{1}{30}$ grain; brandy 1 ounce.

10 a.m. Intravenous quinine 20 grains in 15 ounces of normal saline.

10.20 a.m. Patient improved somewhat during the injection, but collapsed suddenly after receiving 14 ounces of saline. Pulseless and great pallor.

*Treatment.*—Pituitrin 1 c.c., given at once, followed by strychnine $\frac{1}{30}$ grain, and digitalin $\frac{1}{100}$ grain, an hour later.




Case 4. Driver J.

3 p.m. Pulse still very weak, imperceptible at wrist; mental condition alert; temperature 99·2° F.; pulse 134 per min.

*Treatment.*—Champagne hourly.

---

19/9/17—Pulse very much better, but patient still vomiting.

*Treatment.*—Quinine 4 grains, t.d.s., by mouth.

---

29/9/17—Spleen plus and very tender; heart sounds weak, no murmurs; pulse good; temperature normal.

*Treatment.*—Quinine 15 grains, t.d.s., by mouth.

2/10/17—Patient improving.

*Treatment.*—Quinine 10 grains, t.d.s.

16/11/17—Spleen still enlarged and tender; patient still anæmic.

*Treatment.*—Mist. arsen. tonic (graduated doses).

2/12/17—Heart sounds stronger; spleen slightly plus and tender; no anæmia; general condition great improvement.

Patient was sent to England by hospital ship on December 3, 1917.

*Comments.*—The fact that this man collapsed and nearly died after receiving only 14 ounces of saline confirmed my opinion that the saline is to blame for accidents happening when intravenous quinine saline is given.

Since this date, I have made a practice of never using more than 8 ounces of normal saline, and although, in the last four or five months, I have given well over a hundred of these with doses of quinine varying from 20 grains to 40 grains, I have never had any further trouble.

To sum up, I have come to the conclusion :—

(1) That the slow intravenous injection of quinine—20 grains to 40 grains in 8 ounces of normal saline—is the soundest, most scientific and most efficacious method of administering the drug.

(2) That it is quite as safe as any other method. There is no fear of abscess formation or paralysis resulting.

(3) That it should always be used, in the manner I have laid down, in cerebral malaria and all pernicious types of malaria requiring an early and speedy attack by quinine on the parasites in the blood.

(4) That it is a less disagreeable method than any other. Most patients prefer it to the intramuscular injection, as it is less painful at the time, and does not cause stiffness or soreness afterwards.

### (*d*) Quinine per Rectum.

When three or four intramuscular injections have been given into the gluteal region and the patient is still not absorbing the quinine by the mouth, quinine 20 to 30 grains in 8 or 10 ounces of normal saline may be injected very slowly per rectum as an alternative. This is also a very valuable method in :—

(1) Anæmic and cachectic men who are vomiting and have a soft weak pulse.

(2) In cases with thread-like peripheral veins where it is impossible to give an intravenous injection.

(3) In malarial patients who require plenty of fluids. In these, it may be used as an addition to intramuscular quinine and subcutaneous salines.

### Lumbar Puncture.

Before proceeding further, I shall briefly deal with the technique of lumbar puncture.

Although this is useless in the treatment of cerebral malaria, its value from a differential diagnostic point of view is undoubted.

### Technique.

*First Method.*—(1) Place patient on his side near the edge of the bed in a good light.

(2) Thighs should be flexed on abdomen and knees bent; head and shoulders drawn well forward. This increases the spaces between the vertebræ.

(3) Mark the summit of each of the iliac crests. A line joining these marks will pass between the fourth and fifth lumbar vertebræ.

(4) Paint this area with iodine.

(5) Anæsthetize with ethyl chloride.

(6) Use a large-bore needle, carefully sterilized.

(7) Insert the needle with the stilette contained at right angles to the skin in the middle line just below the spine of the fourth lumbar vertebra.

(8) Carefully insinuate it, without using force, in an upward and forward direction through the intervertebral space into the spinal canal. If the point strikes the bone, withdraw slightly and try again. The canal is reached at a depth of 2 to 3 inches.

(9) Withdraw the stilette, and allow the fluid to run into a sterile test-tube, to be examined later at the laboratory.

(10) Continue until the rate of flow is normal—that is, one drop every three seconds.

(11) If a free flow of blood returns through the needle, the point has entered a vein, and the operation must be recommenced.

(12) If no fluid at all, turn the patient further over on to his back, or, if he is conscious, ask him to cough. If no result try another route.

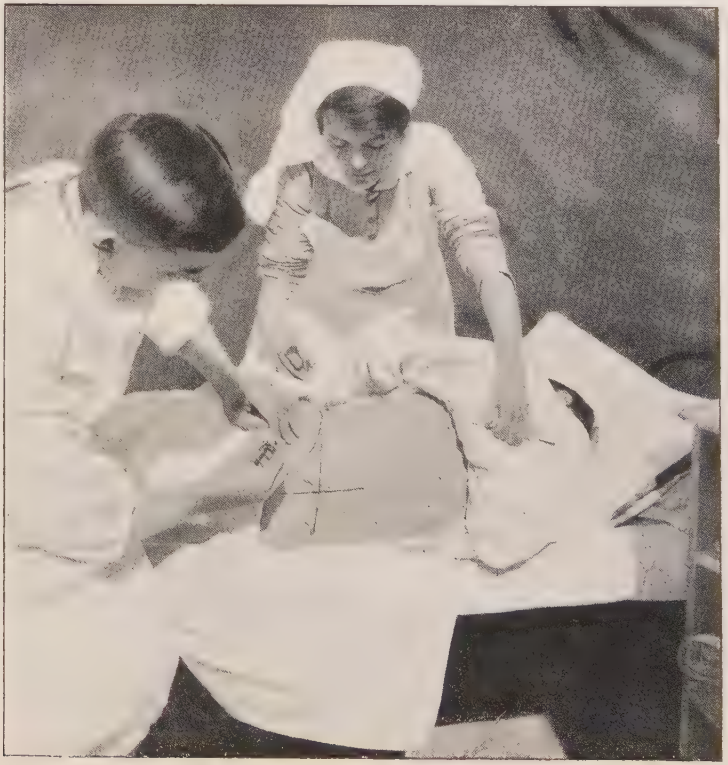
*Indirect Method.*—In this method, the needle is introduced half an inch below, and to the right or left of the spot where the middle line crosses the intercrestal line, the point being directed upwards, forwards and inwards.

NOTE.—(1) *Clear fluid* under pressure with increased polymorphonuclear leucocytes indicates early cerebrospinal meningitis. *Turbid fluid* proves the condition to be very acute. Finding the meningococcus in the cerebrospinal fluid, of course clinches the diagnosis.

(2) *Clear fluid* under pressure with increase of small lymphocytes may mean either syphilitic or tubercular meningitis.

(3) *Clear fluid* under pressure, but normal in character, is obtained in cerebral malaria.

Lumbar puncture. Direct method. (See p. 53.)



Lumbar puncture. Indirect method.

Face p. 54

## CHAPTER V.

## ROUTINE TREATMENT OF MALARIA, AND CEREBRAL MALARIA.

In all cases of malaria or suspected malaria, immediately the patient is seen by the medical officer, a blood film should be taken and sent to the laboratory for examination and report. The only exception should be mild recurrent cases which have been under quinine treatment for some time.

The treatment in such cases is calomel 5 grains, followed later by mag. sulph. and quinine, 15 grains, t.d.s. by the mouth. This may be reduced to quinine 10 grains t.d.s. in benign tertian and quartan cases, after the temperature has been down for ten days, and for a fortnight to a month or more in malignant tertian and all cases which have had repeated relapses.

If the patient is suffering from diarrhœa, castor oil 1 ounce with chlorodyne 15 minims and brandy ½ ounce should be substituted for the calomel.

Every case with an enlarged or tender spleen should be treated promptly with quinine.

Do not keep a patient in bed for more than two or three days after the temperature has become normal. Get him out into the fresh air. This improves his general health and increases his natural powers of resistance. It strengthens his digestive system, assists the action of his bowels and thereby facilitates the rapid absorption of the quinine.

As it is absolutely essential that quinine should be introduced into the circulation at the earliest possible

moment, it is obvious that if a patient is not absorbing it by oral administration, other methods must be resorted to. Therefore, it must be given intramuscularly, intravenously, or by the rectum.

## CEREBRAL MALARIA.

This condition is characterized either by a sudden onset and rapid coma, or by hyperpyrexia, delirium, convulsions and other disturbances of the central nervous system (see Chapter II).

*Rule.*—Every person who has resided in a malarial district and develops disturbances of the central nervous system such as the above, should be promptly treated by the method and with the doses of quinine laid down in this book, even if there is no history of malaria and the parasite has not been found in the blood. This procedure will assist in clearing up the diagnosis if the case is not one of cerebral malaria, and if it is, will save the patient's life.

*Exception.*—If the diagnosis of some other condition is absolute.

### *The Treatment of Cerebral Malaria.*

*Statistics.*—A comparison of the figures in the two periods given below is of interest—

| | No. of cases | Deaths |
|---|---|---|
| First Period: Cerebral malaria in 2,000 cases dealt with in the period immediately *before* the introduction of the "Large dose intravenous and intramuscular method" *Mortality, 57 %* | 7 | 4 |
| Second Period: Cerebral malaria in 2,000 cases dealt with in the period immediately *after* the introduction of this method *Mortality, nil* | 13 | Nil |

It will be noticed that after the introduction of this method, although the number of cases of cerebral malaria was nearly doubled, the mortality was reduced from 57 per cent. to nil.

Voltaire is credited with the cynical remark that "figures can be made to prove anything." This may be true.

I propose now to endeavour to prove my figures by a plain statement of facts. In order to do this, and to show exactly how I arrived at the large dose—intravenous and intramuscular—method of treating acute malaria, and with a view to assisting other medical men to avoid the mistakes I made and to profit by my experience, I shall deal with a sequence of cases in the order they were admitted to this hospital, giving full clinical notes, bacteriological findings, post-mortem reports, &c., and adding comments as I proceed.

CASE 1. *Death from Cerebral Malaria.*—Staff-Sergeant M., aged 41. Service, 1 year 7 months. Admitted on September 24, 1917, at 1.30 p.m.

*On admission.*—Temperature, 103° F., pulse 100. Tried to get out of bed during the afternoon.

4.45 p.m. Better, and spoke quite rationally; said he had been ill for a week. Heart and lungs: Normal. Spleen: Plus and tender. Blood film: M.T. crescents.

*Treatment.*—Calomel 4 grains, mist. alb. 1 ounce, mane. Quin. sulph. 15 grains, by mouth.

---

*Progress.*—25/9/17—

6 a.m. Slept well during the night. Temperature, 98° F.; pulse 84 per minute, and full.

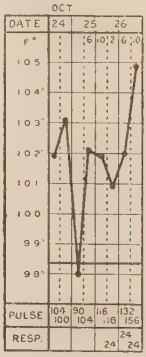
9 a.m. Does not look so well.

*Treatment.*—Quinine, 15 grains by mouth—retained.

10.30 a.m. Suddenly became worse, and could only be roused with difficulty to answer questions. Temperature, 98·4° F.; pulse 90.

*Treatment.*—

11 a.m. Intramuscular quinine, 20 grains; brandy, 1 ounce, 4-hourly.
2 p.m. Pituitrin, 1 cubic centimetre.
3 p.m. Rectal saline 1½ pints—retained.
6.50 p.m. Lumbar puncture—4 ounces of clear spinal fluid under high pressure drawn off.
8.30 p.m. Intramuscular quinine, 20 grains.
11 p.m. Pituitrin, 0·5 cubic centimetre.




Case 1. Staff-Sergeant M.

26/9/17.—Patient remained comatose all night, and was unable to take nourishment or stimulants by the mouth.

10 a.m. Temperature, 105° F., pulse 126 per minute.
Noon. A second lumbar puncture, but very little spinal fluid obtained. Still comatose.

*Treatment.*—

7.30 a.m. Strychnine $\frac{1}{60}$ grain, digitaline $\frac{1}{100}$.
10 a.m. Rectal saline—not retained.
12.30 p.m. Intramuscular quinine, 40 grains.
Died at 1.30 p.m.

*Post-mortem Report.*—Brain: Petechial hæmorrhages

over cerebrum; congestion of surface vessels; minute petechial hæmorrhages peppered throughout the substance of the cerebrum and cerebellum.

Heart: Muscles soft and atrophic; cavities dilated; no valvular disease.

Lungs: Congestion at both bases.

Spleen: Four times normal size, very soft and dark.

Liver: Large, soft and bile-stained.

Gall-bladder: Distended.

Duodenum: Bile-stained.

Kidney: Some congestion.

*Report on section of brain* sent to the Base Laboratory for examination: "Cerebral thrombosis due to malarial parasites; foci of hæmorrhages and necrosis of brain tissues."

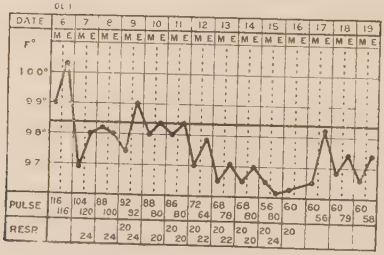
*Comments.*—(1) The post-mortem report on the condition of the heart, "muscle soft and atrophic, cavities dilated," bears out my arguments that a large quantity of fluid injected intravenously is dangerous. By over-dilating the organ it causes stoppage of its action, the thin-walled atrophic and atonic muscle not being able to contract and expel the cardiac contents.

(2) I have observed in quite a number of cases of cerebral malaria that the first indication of the condition was an attempt on the part of the patient to get out of bed.

(3) The treatment was inadequate. He received quinine 15 grains by the mouth in the first eighteen hours instead of the 80 or 100 grains intravenously and intramuscularly in the first twelve hours which he would have received had he been admitted a month later. Quinine 40 grains intramuscularly and 15 grains by the mouth on the second day with no intravenous at all was again insufficient. The 40 grains intramuscularly given an hour before his death was waste of quinine.

This result proved to me that there was something radically wrong with my treatment of cerebral malaria, so I determined to give larger doses of quinine a trial in the next case that came under my charge. The opportunity arrived ten days later.

CASE 2. *Recovery after an attack of Cerebral Malaria.*—Saddler G., aged 41. Service, 2 years 8 months. Diagnosis: Cerebral malaria. Admitted on October 6, 1917. In Balkans, 9 months.




Case 2. Saddler G.

Onset of present illness, September 30, 1917.

*Symptoms.*—Headache, backache, shivering, sweating and vomiting.

*On admission.*—Temperature, 99° F., pulse 100; tongue dry and furred; heart sounds feeble, reduplicated second pulmonary. Anæmia and jaundice.

*Treatment.*—Calomel and mag. sulph.

*Progress.*—7/10/17 — Patient semicomatose. Temperature 97° F., pulse 104.

10 a.m. Tongue, dry and furred.

9 p.m. Much improved but still drowsy. Temperature 98·4° F., pulse 100.

*Treatment.*—

10 a.m. Intramuscular quinine, 20 grains.

1.30 p.m. Intravenous quinine, 20 grains.

7 p.m. Intramuscular quinine, 20 grains.
9.30 p.m. Intramuscular quinine, 20 grains.
Patient also had pituitrin, 1 cubic centimetre, and strychnine, $\frac{1}{30}$ grain.

---

8/10/17—Patient much better. Temperature, 98·4 °F.; pulse 100. Clear mentally.
*Treatment.*—Intramuscular quinine, 20 grains; quin. sulph., 15 grains, t.d.s., daily.

---

12/10/17—Improvement continues. Anæmic. Temperature normal; pulse 74 per minute.

---

14/10/17—Quinine reduced to 30 grains a day.

---

1/11/17—Walking about but still anæmic.
*Treatment.*—Quinine 30 grains daily still continued. Iron and arsenic tonics given.

---

17/12/17—Patient evacuated. Temperature has been normal since the day after admission. Has had no relapse.

Amount of quinine received by him to date, 1,800 grains.

*Personal statement* of Saddler G., after recovery from an attack of cerebral malaria: "I remember coming down from Karasouli and arriving at the station. I remember carrying my kit to an ambulance, and then I fell down and an officer ordered me to be put on a stretcher. I cannot remember anything more until I was in bed in hospital and someone was washing me. The next thing I remember was showing my tongue to the Colonel—I think it was—and I had a very nasty taste in my mouth. Then I remember someone giving me an injection into my back at night. I cannot remember anything being run into my arm by a long tube,

but I remember waking up one morning and finding a bandage on my arm. After this, I remember waking up from time to time and seeing things in the ward. I couldn't hardly speak when I came round and saw the sisters. My speech gradually got better, and I think this was on the third day or the fourth day after I came into hospital. After that, I can remember quite well.

"A. J. G., *Saddler.*

"Witnesses:

"JOHN CLAYTON,

"*S.C.F. (U.B.)*,

"REGINALD J. DICKSON,

"*C.F. (C. of E.)*"

*Comments.*—This was the first case in which fairly large doses of quinine were given over a short period of time by the intravenous and intramuscular method.

Saddler G. received 80 grains within twelve hours on the first day, and 65 grains the following day.

After he had been given 60 grains on October 7, 1917, the medical officer in charge of the ward refused to administer any more of the drug, and appealed to the commanding officer of the hospital. The colonel supported me, and the patient got the treatment I determined upon. This was the turning point. I must say this, however, for the medical officer in question, that being also the hospital opthalmologist, he had visions of quinine amaurosis, and for that reason his attitude was justifiable.

I regret to say that, notwithstanding the experience I had in the case of Saddler G., I lost the next two cerebral malaria patients through lack of the necessary moral courage to follow up my success.

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CASE 3. *Death from Cerebral Malaria.*—Rifleman M., aged 42. Service, 6 months. Admitted on October 15, 1917. No history of previous malaria.

Onset of present illness: October 11, 1917.

*Symptoms.*—Headache, giddiness, pains in back and legs, shivering, sweating, weakness. No vomiting.

*On admission.*—Pulse regular, tongue dry and furred, heart sounds weak, spleen palpable but not tender.

*Blood film.*—Benign tertian rings.

*Treatment.*—Quinine sulph., 15 grains, t.d.s.

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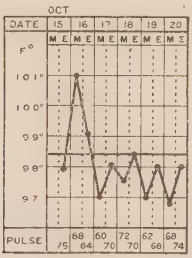
*Progress.*—16/10/17—Temperature, 101° F.; tongue dirty. Patient complains of feeling nauseous and says that his head feels "a little cloudy."




Case 3. Rifleman M.

12 noon. Put on "Dangerously Ill" list.

7 p.m. Speech confused; drowsy. Seen by Officer in Charge of Medical Division.

12 midnight. Temperature 99·2° F.; patient vomited; mental condition the same.

*Treatment.*—

12 noon. Intramuscular quinine, 20 grains.

7 p.m. Intramuscular quinine, 20 grains.

12 midnight. Intramuscular quinine, 20 grains.

---

17/10/17—Brandy, 1 ounce, s.o.s. Temperature, 97° F.; pulse 60 per minute, variable in strength; mentally clearer, but still heavy and deaf.

*Treatment.*—

9.15 a.m. Strychnine, $_1$ grain.
12.30 p.m. Intramuscular quinine, 20 grains.
10 p.m. Intramuscular quinine, 20 grains; champagne, 1 ounce, s.o.s.

---

18/10/17—Restless and inclined to be delirious; pulse stronger.
3 p.m. Restless and violent.
10.45 p.m. Stertorous breathing for about fifteen minutes.

*Treatment.*—

11 a.m. Intramuscular quinine, 20 grains.
4 p.m. Morphia, $\frac{1}{4}$ grain hypodermically.
6 p.m. Intramuscular quinine, 20 grains.
10.45 p.m. Strychnine, $\frac{1}{30}$ grain.
11 p.m. Intramuscular quinine, 20 grains.
11.45 p.m. Morphia, $\frac{1}{4}$ grain hypodermically.

---

19/10/17—*Notes by Officer in Charge Medical Division.*—"Patient semi-conscious; knee-jerks exaggerated, particularly right; ankle-jerks exaggerated slightly; supinator-jerks brisk and equal; plantar reflexes extensor; pupils normal in size, react to light; ankle clonus marked; abdominal reflexes normal."

10.30 p.m. Lumbar puncture: Fluid under considerable pressure, ran freely; about 20 cubic centimetres removed. Patient improved; makes efforts at speech; hears and understands.

4 p.m. *Notes by Colonel Purves Stewart, Consulting Physician.*—"Stuperose, but puts out tongue on request; moves all limbs to

order; plantars now flexor; abdominal reflexes brisk; ankle clonus, right side only; grimaces with left side of face more and appears to move left hand more than right; pulse feeble."

12 midnight. Patient unconscious; respirations 32 per minute and stertorous at times.

---

*Treatment.*—

10.45 a.m. Intravenous quinine, 20 grains in 10 ounces of saline.

6.30 p.m. Intravenous quinine, 20 grains in 10 ounces of saline.

12 midnight. Intramuscular quinine, 20 grains.

---

20/10/17—Patient worse; coma deepening; respirations shallow, air-hunger type; urine, trace of albumin, no sugar; can hardly swallow.

4 p.m. Deeply comatose; incapable of swallowing. Died at 5 p.m.

*Post-mortem Report.*—Brain: Surface œdematous. Whole substance of the brain peppered with petechial hæmorrhages.

Spleen: Very adherent; perisplenitis. Three times normal size; very soft; semi-liquid and very dark in colour.

Liver: Enlarged and fatty; some perihepatitis.

Heart: Some dilatation—muscle firm to feel.

Aorta: Early senile atheroma.

Lungs: Congestion and œdema most marked in lower lobes.

*Note.*—(1) The condition of the brain, heart, spleen and liver.

(2) That the blood film was returned as "benign tertian rings found."

*Résumé.*

| | Condition | Treatment | | |
|---|---|---|---|---|
| 16/10/17 | Speech confused; patient drowsy | Three I.M.Q. injections | = 60 | grains |
| | | Quinine by mouth | = 15 | ,, |
| | | | 75 | ,, |
| 17/10/17 | Mentally clear ... | Two I.M.Q. injections | = 40 | ,, |
| 18/10/17 | Restless and delirious | Three I.M.Q. ,, | = 60 | ,, |
| 19/10/17 | Semi-comatose ... | Two I.V.Q. ,, | = 40 | ,, |
| | | One I.M.Q. injection | = 20 | ,, |
| | | | 60 | ,, |
| 20/10/17 | Comatose ... ... | No quinine given | = 20 | ,, |
| | Total amount of quinine = 235 grains | | | |
| | Daily average = 59 ,, | | | |

*Comments.*—A most instructive case showing—

(1) How not to treat cerebral malaria.

(2) That notwithstanding the administration of 235 grains of quinine in four days, the patient succumbed.

(3) That two intravenous and nine intramuscular injections were of no avail.

(4) That after receiving 75 grains, the patient was "mentally clear" on the next day.

(5) That instead of following this up with larger doses, the quinine was reduced to 40 grains on October 17, 1917.

(6) That the amount of quinine given being insufficient, the patient gradually became comatose, and died.

I am of opinion that had he received 80 to 120 grains of quinine by the intravenous and intramuscular method I now use, followed by further injections of rather smaller doses as required, he would have recovered.

Reference to the case of Sergt. G., or any of the other patients who recovered after treatment by this method, will prove whether I am right or wrong (see p. 78).

To achieve success it is absolutely essential to push

the quinine in the early stages of the disease, and not to be afraid either of the drug or of the method of administration.

It may be of interest to mention in passing that the Medical Officer in Charge of the ward refused to believe that this patient was suffering from cerebral malaria, and contended that the doses I instructed him to use were dangerous.

He profited, however, by this experience, and immediately afterwards was put in charge of the intravenous wards. He has assisted me ever since in the treatment of nearly all the cerebral and pernicious malarial fevers admitted to the hospital, and thinks nothing of giving 100 grains of quinine intravenously and intramuscularly in twelve hours, and following this up with further large doses.

I am referring to this change of attitude on his part to show how difficult it is for a medical officer, even if he has had considerable experience, to make up his mind to give the large quantities of the drug necessary in these cases.

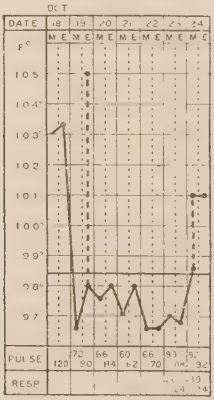
I shall now proceed to give details of the last case of cerebral malaria which died in this hospital. The only excuse I have to offer for my failure to save him is that he presented symptoms that were quite new to me. I was still groping in semi-darkness, and had not quite grasped the fact that malaria is capable of causing almost any disturbance of the central nervous or, for the matter of that, of every other system of the human body. Nor had I quite realized that quinine, properly and scientifically administered in sufficient dosage, is more than a match for the malaria parasite and its toxins.

CASE 4. *Death from Cerebral Malaria.*—Private R., aged 25. Service, 3 years. Admitted on October 18, 1917. No previous malaria.

Onset of present illness, October 15, 1917.

*Symptoms.*—Rigors and vomiting.

*On admission.*—Temperature, 103·5° F.; pulse 120 per minute, soft, regular; herpes labialis; tongue moist, white fur; eyes congested; no jaundice; heart sounds muffled; lungs normal; liver tender; spleen plus; urine no trace of albumin; no vomiting.




Case 4. Private R.

*Blood film:* Benign tertian parasites found (Schüffners' dots).

*Treatment.*—Calomel 5 grains; mag. sulph. 2 ounces. mane; quinine, 15 grains, t.d.s., daily.

---

19/10/17—Temperature sub-normal; pulse 72 per minute, good volume.

p.m. Rigor; temperature, 105° F.; pulse 90.

---

20/10/17—Improvement; temperature normal; pulse 66.

p.m. Patient got out of bed; slight rigor; sweating, *but no rise of temperature.*

---

22/10/17—Patient sweated freely; rigidity of arms and legs, condition passed off in ten minutes; *no loss of consciousness; no rise of temperature;* pulse soft.

12 noon. Perspiring freely, arm semiflexed, legs somewhat rigid; utters occasional short cries; appears to be hysterical; can extend arms when told to, but they return to flexed position immediately afterwards; no loss of consciousness; has not bitten tongue; no rise of temperature; pulse soft and fast; pupils moderately dilated and react to light; respirations rapid and stertorous; attack lasted fifteen minutes.

*After attack.* Quite flaccid; took fluids and quinine by the mouth; no vomiting; knee and ankle-jerks absent; no mental symptoms.

2 p.m. Sleeping.

6 p.m. No further attacks; sweated considerably; tongue dry with white fur; bowels constipated; temperature normal; pulse good.

*Treatment.*—

9 a.m. Intramuscular quinine, 20 grains.

12.30 p.m. Intramuscular quinine, 20 grains; quinine, 15 grains, t.d.s., continued.

---

23/10/17—12.30 a.m. Another similar attack, given brandy.

4 a.m. A further slighter attack, after which patient slept.

9 a.m. Temperature, 97° F.; pulse 90; respirations 20; patient rather drowsy; no other mental symptoms.

11.30 a.m. Sweating severely, but no rigor; convulsive movements of arms and legs followed by rigidity; respirations rapid; patient conscious, and during attack asked for bed-pan, bowels moved; attack lasted for five minutes.

1.30 p.m. Tongue and lips dry; complains of thirst; subcutaneous saline of two pints given; pulse improved.

3.30 p.m. Another attack.

6.30 p.m. A further attack with contractions more marked; no rise of temperature; respirations rapid; perspired freely.

8.30 p.m. Temperature normal; pulse 115 per minute; respiration 30; patient has retained quinine by mouth as well as plenty of nourishment and fluids; bowels, free; has had no rise of temperature during any of the attacks.

*Treatment.*—

8.30 a.m. Intramuscular quinine, 20 grains; quinine, 15 grains t.d.s. by mouth; morphia, $\frac{1}{4}$ grain hypodermically.

---

24/10/17—Slept until 4.30 a.m., after which he sweated freely.

8.30 a.m. Sweating; temperature normal; pulse 96 per minute, soft; respirations 30 per minute; abdomen tense, tympanitic; rigidity of arms more marked, assumed "pugilistic attitude," but can straighten arms voluntarily; no retraction of head; reflexes normal.

10.30 a.m. Temperature, 101° F.; vomited; sweating less.

2 p.m. Lumbar puncture, clear fluid not under pressure; bacteriological report, "fluid clear, sterile, six cells per cubic millimetre."

2.30 p.m. Vomited green fluid; abdomen distended and tympanitic, long tube passed *per rectum* gave relief.

5 p.m. Temperature, 101° F.; pulse good; patient has no pain.

8 p.m. Collapsed suddenly and died at 8.45 p.m.

*Treatment.*—

2 p.m. Intramuscular quinine, 20 grains; no oral quinine given, due to vomiting.

8 p.m. Pituitrin, 1 cubic centimetre.

8.30 p.m. Strychnine, $\frac{1}{60}$ grain; digitaline, $\frac{1}{100}$ grain.

An attempt was made by the Officers in Charge, Medical and Surgical Divisions, to give an intravenous quinine, but patient died before the needle had been introduced.

*Post-mortem Report* —Brain: Scattered petechial hæmorrhages throughout substance of brain—most marked in frontal regions, but nowhere extreme. Membranes were normal.

Heart: Fatty and atrophic. Aortic and pulmonary valves show post-mortem staining. No inflammation.

Lungs: Apical tuberculosis in both lungs. Half of each upper lobe consolidated and showing numerous caseated and calcified nodules. Apex of left lower lobe also slightly involved.

Liver: Enlarged and fatty.

Spleen: More than twice normal size, dark in colour and soft. Kidneys and other organs normal.

*Comments.*—Note the following points:—

(1) That there was no rise of temperature during any of the attacks. It rose to 101° F. a few hours before his death.

(2) The contraction of the limbs—which could be voluntarily straightened.

(3) That an early symptom was an attempt to get out of bed.

(4) That throughout he never lost consciousness or the control of his sphincters.

(5) In this case and the one preceding it (Rifleman M.), the blood films were returned as benign tertian. This is interesting because the view generally accepted is that only the malignant tertian parasite can cause cerebral malaria.

(6) That the post-mortem report states that the petechial hæmorrhages were most marked in the frontal lobes.

The treatment was of course quite inadequate; quinine, 45 grains a day, given to a patient with a dirty tongue was of very little use. The same may be said of the four intramusculars spread over a period of six days.

The net result of all these catastrophes, however, was that after this I introduced the intravenous wards, into which every patient who showed any sign of pernicious malaria of any kind whatsoever was immediately transferred. Here he was under my constant supervision and received treatment by the large-dose intravenous and intramuscular method without any delay. Since this date I have had no deaths from cerebral malaria.

### Cases of Recovery from Cerebral Malaria.

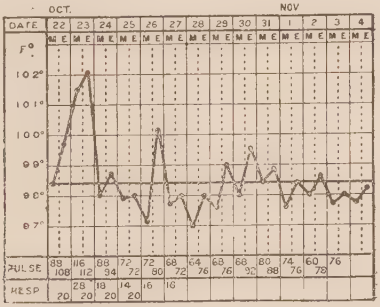
Thirteen cerebrals were admitted after October 20, 1917, and all recovered.

Case 5.—Sergt. G., aged 31. Service, 3 years. Admitted on October 22, 1917, at 11 a.m. Diagnosis: Cerebral malaria. In Balkans, 1 year 11 months.

*Previous history.—Notes from Field Ambulance:* "Patient complains of pain in back of head; vomiting; ill for

six days, first attack; jaundiced; liquid motions for last few days." *Notes from C.C.S.:* "No malaria previously; very asthenic; skin icteric tinge; spleen plus and tender; urine normal.

*On admission.*—Comatose. Placed on D.I. list. Temperature normal; pulse 88, regular and fairly good; no speech, only response to questions is a slow opening of eyes; conjunctival and corneal reflexes present; pupils do not react to light; skin icteric tinge; heart sounds muffled; spleen plus. *First blood film:* Malignant tertian rings and crescents; heavy infection.




Case 5. Sergeant G.

*Progress.*

11.30 a.m. Slight response to needle-prick when giving intravenous, some improvement following.

3 p.m. Improved; responds better to request to put out tongue; tongue very dirty and dry; pulse better, no Kernig's sign; knee-jerks difficult to obtain; slight ankle clonus; plantar reflexes flexor.

6 p.m. Pulse 99, temperature 100° F.; patient about the same.

11 p.m. Still quite drowsy: slight response to stimuli; unable to swallow.

*Treatment.*—22/10/17—

11 a.m. Intramuscular quinine, 20 grains.

11.30 a.m. Intravenous quinine, 20 grains, in normal saline, 10 ounces.

3 p.m. Intravenous quinine, 20 grains, in normal saline, 10 ounces.

6 p.m. Intramuscular quinine, 20 grains.

11.30 p.m. Intramuscular quinine, 20 grains.

---

23/10/17—Temperature, 101·6° F., pulse 116.

10 a.m. Patient improving, makes efforts at speech; taking a little fluid nourishment.

6 p.m. Temperature, 102·6° F., pulse better; tongue very dirty.

*Treatment.*—

11 a.m. Intravenous quinine, 20 grains, in normal saline, 8 ounces.

6 p.m. Intravenous quinine, 20 grains, in normal saline, 8 ounces.

11 p.m. Intravenous quinine, 20 grains, in normal saline, 8 ounces.

---

24/10/17—10 a.m. Patient much better, still drowsy; taking nourishment well, and is able to speak.

6 p.m. Temperature normal; improvement.

*Treatment.*—

11 a.m. Intramuscular quinine, 20 grains.

7 p.m. Intramuscular quinine, 20 grains.

---

25/10/17—Patient better in every way; taking nourishment well.

*Treatment.*—

10.30 a.m. Intramuscular quinine, 20 grains, and quinine, 15 grains, t.d.s., by mouth commenced.

---

26/10/17—Temperature rose to 100·2° F.; but patient feels quite well.

*Treatment.*—Quinine, 15 grains, t.d.s., by mouth.

---

27/10/17—Temperature normal; patient improving, and takes his quinine, 15 grains, t.d.s., well, by mouth.

---

28/10/17—Temperature normal; making good progress.

*Treatment.*—Intramuscular quinine, 20 grains, given to prevent another rise of temperature; and quinine, 15 grains, t.d.s., by mouth continued.

---

29/10/17—Improvement continues.

*Treatment.*—Quinine, 45 grains, daily.

---

6/11/17—"Up" to-day. Evening temperature, 99° F.

---

13/11/17—Some pain in left hip at seat of intramuscular injections; no redness or signs of sepsis.

---

*Treatment.*—

15/11/17—Quinine reduced to 30 grains daily.

---

16/11/17—Pain gone from hip; patient doing excellently.

---

17/12/17—*Second blood film:* Malignant tertian, young trophozoites.

Patient discharged to a convalescent depot. Appearance full-blooded. He stated he had never felt better in his life.

---

*Personal statement* of Sergeant G., after recovery from cerebral malaria: "I remember a sergeant stating to me that 'your haversack is on the stretcher, sergeant.' As far as I can remember it was getting dusk at the time on the evening of October 20, 1917, at R——, the Battalion Headquarters. I cannot remember anything after that. I can't remember being carried on the stretcher to the dressing station. The next thing I remember was Mr. Robertson coming to my bed in the 28th General Hospital. Lieutenant Robertson said he was coming to give me another injection here in the hip, but I cannot remember the day or date. After that I came right round to my senses and can remember everything.

"J. G., *Sergeant.*

"Witnesses:

"T. W. ARNISON, *Lieutenant, R.A.M.C.*

"W. L. ANDREWS, *Sister* (*T.F.N.S.*).

"— *General Hospital,*

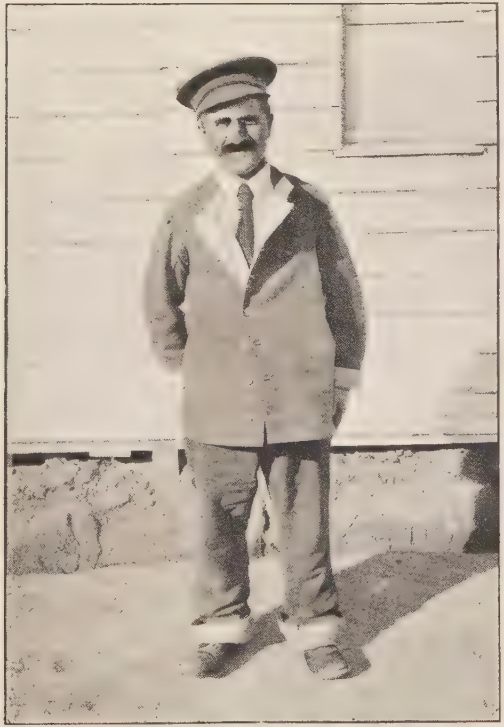
"*December* 14, 1917."

*Comments.*—(1) This is the correct way to treat cerebral malaria.

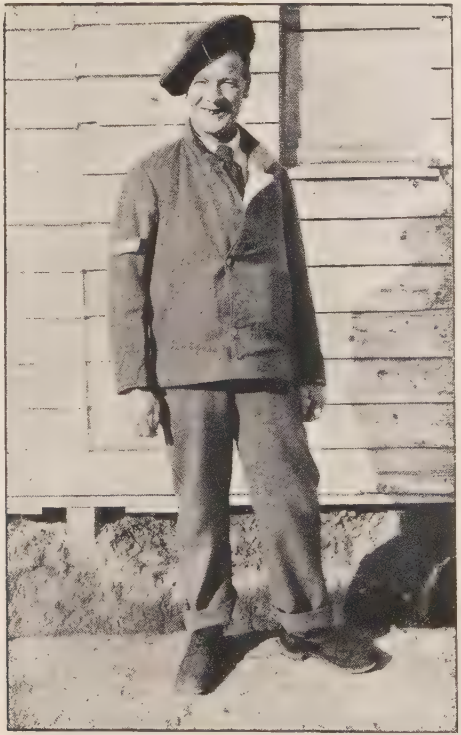
(2) This patient was comatose for three days, during which time, as he himself states, he was unable to remember anything that happened.

(3) Although comatose on the day of admission to this hospital, his temperature was normal, and his pulse regular and fairly good—rate 88 per minute.

(4) The rise of temperature on October 26, 1917, was probably due to his not absorbing the quinine by the



CASE 2.—Saddler G. After recovery from cerebral malaria. (See p. 60.)



CASE 5.—Sergeant G. After recovery from cerebral malaria.

Face p. 76

mouth. Unfortunately there is no note in regard to the condition of his tongue on that date.

(5) The result of the first blood film (malignant tertian rings and crescents) shows how serious the condition was.

(6) It is interesting to find young trophozoites in the second blood film on December 17, 1917—two months after the acute attack—in spite of the amount of quinine he had had. This indicates that a heavy infection by the malignant tertian parasites requires a prolonged course of treatment by fairly large doses of quinine (30 to 45 grains a day).

The total amount of quinine received by him in fifty-six days was 1,880 grains—daily average, 34 grains.

A further extensive dosage with quinine and a change to another climate would be required to effect a cure in this case.

*Résumé of Case in Acute Stage.*

| | Condition | Treatment |
|---|---|---|
| 22/10/17 | 11 a.m. Comatose | 11 a.m. I.M.Q., 20 grains. |
| | | 11.30 a.m. I.V.Q., 20 ,, |
| | 3 p.m. Improvement | 3 p.m. I.V.Q., 20 ,, |
| | | 6 p.m. I.M.Q., 20 ,, |
| | 11 p.m. Semicomatose | 11.30 p.m. I.M.Q., 20 ,, |
| 23/10/17 | Still drowsy. Makes efforts at speech | Three I.V.Qs., 60 grains. |
| 24/10/17 | Still drowsy, but able to speak | Two I.M.Qs., 40 grains. |
| 25/10/17 | Clear mentally ... | One I.M.Q., 20 grains.<br>Oral quinine, 45 grains daily. |

Patient received quinine, 100 grains intravenously and intramuscularly, within a period of twelve hours on the first day.

He had quinine, 160 grains—five intravenous and three intramuscular injections—in the course of the first thirty-six hours.

A comparison of the treatment in this case with that of Rifleman M., on p. 66 is highly instructive, showing as it

does, the extraordinary advance made in regard to quinine dosage within the space of one week.

| | Rifleman M. | Sergeant G. |
|---|---|---|
| *On admission* | Drowsy. Gradually got worse and became comatose at the end of the fourth day. | Comatose. Gradually improved, and was mentally clear on the fourth day. |
| *Treatment* ... | An irregular administration of quinine — average 60 grains a day, chiefly intramuscularly. Intravenous injections not given until the fourth day. | Quinine 100 grains intravenously and intramuscularly within 12 hours on the first day. Intravenous quinine 60 grains on the second day. |
| *Result* ... | Death. | Recovery. |

*Comments.*—(1) Rifleman M. had a far better chance of recovery than had Sergeant G., as he only reached the state of coma on the fourth day, which the latter was in when admitted.

(2) The comparison of the stages from drowsiness to death and from coma to recovery is very striking.

Case 6. *Recovery from Cerebral Malaria.*—Pioneer R., aged 44. Service, 1 year 4 months. Admitted on October 21, 1917.

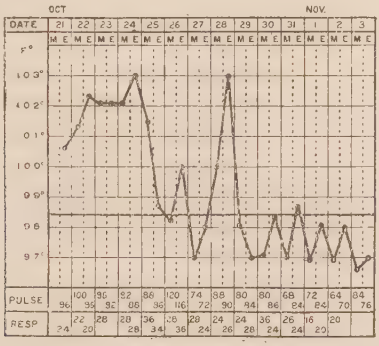
*Previous history.*—Malaria in July, 1917.

*Onset of present illness.*—October 20, 1917.

*Symptoms.*—Headache and shivering; patient was on his way home and collapsed on the boat.

*On admission.*—Appears to be older than stated age; is rather confused when answering questions and is inclined

to be verbose ; no delirium ; temperature, 100·6° F. ; pulse good, regular ; skin sallow ; tongue rather dry and furred ; heart : systolic bruit accompanying first sound in mitral area ; lungs : signs of bronchial catarrh and definite pleurisy at right base, very rough friction ; spleen : palpable, not tender.




Case 6. Pioneer R.

*Blood film :* Benign tertian parasites (rings).

*Treatment.*—Intramuscular quinine 20 grains, and quinine sulph. 20 grains, by mouth ; stimulants s.o.s.

22/10/17—Temperature, 101° F. ; tongue cleaner and more moist. Evening temperature, 102·6° F. ; pulse 100 ; respirations 22 per minute ; pleurisy about the same.

*Treatment.*—Quinine sulph. 15 grains, t.d.s., by mouth ; brandy, 1 ounce 4-hourly.

---

23/10/17—Temperature, 102·4° F. ; pulse 96 ; respirations 28. Lungs : pleuritic friction over whole of right lower lobe, slight impairment of resonance ; sputum scanty, not rusty ;

cough troublesome. Condition suggests a pneumonic patch in underlying lung, but no definite physical signs.

*Treatment.*—Quinine 15 grains, t.d.s.

---

24/10/17—Temperature, 102·4° F. in morning; evening temperature, 103° F.; patient inclined to be delirious.

10 p.m. Temperature, 100° F.; sweating profusely. Put on D.I. list.

*Treatment.*—Quinine sulph. 15 grains, t.d.s., by mouth; mist. pot. iod. and creosote, 4-hourly.

---

25/10/17—Tongue dry; patient sweating; sputum: fair amount, mucopurulent.

6 p.m. Temperature, 98·6° F.; perspiring freely; pulse fair; respiration very shallow, assuming Cheyne-Stokes character. Patient very drowsy and picks at bed clothes. Obviously dying.

8.30 p.m. Patient revived somewhat; breathing better; becoming restless and delirious.

*Treatment.*—

10 a.m. Intramuscular quinine 20 grains.

6 p.m. Intramuscular quinine, 20 grains; strychnine $\frac{1}{30}$ grain hypodermically; rectal salines, 10 ounces, 2-hourly, and brandy, $\frac{1}{2}$ ounce, 2-hourly, ordered; atropine sulph. $\frac{1}{100}$ grain hypodermically.

8 p.m. Intravenous quinine, 20 grains in normal saline 8 ounces.

---

26/10/17—Patient very restless during night.

9 a.m. Still restless and rambling but a little more sensible in his talk than yesterday.

Evening temperature, 100° F.; pulse, 116; respirations 26. Patient worse, very restless and delirious; after intravenous and intramuscular, slept for a few hours.

*Treatment.*—

2 a.m. Morphia ¼ grain, hypodermically.
10 a.m. Intravenous quinine 20 grains in normal saline 8 ounces.
3 p.m. Intravenous quinine 20 grains in normal saline 8 ounces.
6 p.m. Morphia ¼ grain, hypodermically.
9.30 p.m. Intravenous quinine 20 grains in normal saline 8 ounces.
10 p.m. Intramuscular quinine 20 grains.

---

27/10/17—7 a.m. Pulse rather weak; strychnine $\frac{1}{30}$ grain hypodermically, given.
9 a.m. Temperature, 97° F.; pulse 76, good; patient drowsy this morning, quiet, when roused is a little more rational in his talk.

*Treatment.*—

11 a.m. Intramuscular quinine 20 grains.
6 p.m. Intramuscular quinine 20 grains.
9 p.m. Intravenous quinine 20 grains, in saline 8 ounces.

---

28/10/17—Pulse good; mental condition good; more sputum, rather offensive. Evening temperature, 103° F.; condition same.

*Treatment.*—Mist. pot. iod. and creosote resumed.

11 a.m. Intramuscular quinine 20 grains.
6.30 p.m. Intravenous quinine 20 grains, in saline 8 ounces.

10.30 p.m. Intramuscular quinine 20 grains.

29/10/17—Patient seems much better; temperature normal; pulse 80; respirations 24; tongue dry and furred.

*Treatment.*—

10 a.m. Intramuscular quinine 20 grains.

6.30 p.m. Intravenous quinine 20 grains, in saline 8 ounces.

---

30/10/17—Improvement.

*Treatment.*—

10.30 a.m. Intramuscular quinine 20 grains.

3.30 p.m. Intravenous quinine 20 grains, in saline 8 ounces.

---

31/10/17—Cough still troublesome; tongue cleaner and more moist; no vomiting.

*Treatment.*—

10 a.m. Intramuscular quinine 20 grains, quinine sulph. 15 grains, t.d.s., by mouth daily.

---

22/11/17—Patient making good progress, and was boarded on this date in order to be sent to England.

---

9/12/17—Quinine reduced from 45 grains to 30 grains a day; total amount of quinine taken was 2,715 grains in seventy days; average 39 grains a day.

---

*Résumé.*

| | Condition | Treatment |
|---|---|---|
| 21/10/17 | Confused and verbose ... | Quinine, 40 grains—one I.M.Q. |
| 22/10/17 | Pleurisy ... ... ... | Quinine, 65 grains—one I.M.Q. |
| 23/10/17 | ? Pneumonic patch ... ... | Quinine, 45 grains—oral. |
| 24/10/17 | Delirious ... ... ... | Quinine, 45 grains—oral. |
| 25/10/17 | 6 p.m. Very drowsy and picking at bedclothes. Obviously dying.<br>8.30 p.m. Restless and delirious | Quinine, 60 grains—two I.M.Qs. and one I.V.Q. |
| 26/10/17 | 10 a.m. Delirious and rambling.<br>9.30 p.m. Very restless and delirious | Quinine, 80 grains—three I.V.Qs. and one I.M.Q. |
| 27/10/17 | Drowsy, but when roused is more rational | Quinine, 60 grains—one I.V.Q. and two I.M.Qs. |
| 28/10/17 | Mental condition good ... | Quinine, 60 grains—one I.V.Q. and two I.M.Qs. |
| 29/10/17 | Tongue dry and furred ... | Quinine, 40 grains—one I.V.Q. and I.M.Q. |
| 30/10/17 | Tongue still dry ... ... | Quinine, 40 grains—one I.V.Q. and one I.M.Q. |
| 31/10/17 | Tongue moist and clean ... | Quinine, 45 grains, continued daily. |

*Personal statement* of Pioneer R., after cerebral malaria. —"I remember coming into hospital on the evening of Sunday, October 21, 1917. I remember being shy of the Sisters the following day. After that I remember nothing until I woke up and found a man sitting on my bed reading 'The Balkan.' I asked him what time it was, and he said 'ten-thirty.' I then asked him what day it was, and I think he said Tuesday. I then asked him the date, and he said 'October 30,' and gave me the paper to see. After that I remember everything.

"T. R.

"Witnesses:

"F. M. HOBBS, *Q.A.I.M.N.S. (R.) Sister.*

"R. ROBERTSON, *Lieutenant, R.A.M.C.*

"— *General Hospital,*

"*December* 15, 1917."

*Comments.*—(1) Note the age, the pulmonary complication and the fact that the slide was returned as benign tertian rings.

(2) This case is interesting because the patient owes his recovery to the experience I got in the treatment of Sergeant G. Pioneer R. was admitted the day before Sergeant G. (October 21, 1917).

I was so fully occupied with Cases Nos. 4 and 5 (Private R. and Sergeant G.) that I did not realize how bad Pioneer R. was until the medical officer informed me that he was dying. This was on October 25, 1917, the day Sergeant G. recovered consciousness and was on the road to recovery. I then took a hand in the treatment, and gave Pioneer R. 120 grains of quinine—four intravenous and two intramuscular—in twenty-six hours, and followed this up with further intravenous and intramuscular injections as shown above.

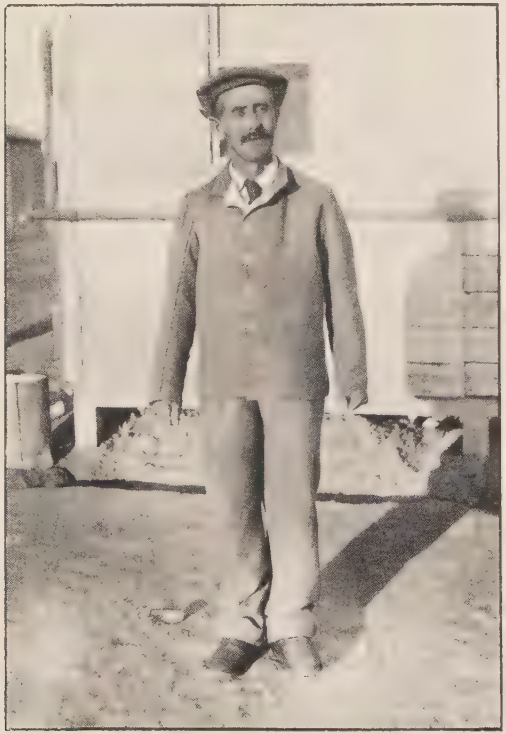
(3) The treatment from 8 p.m. on October 25, 1917, onwards, is an object lesson on how to deal with cerebral malaria, even when the case appears to be hopeless.

(4) According to his own statement the patient remembers nothing for eight days—from October 22 to October 30, 1917.

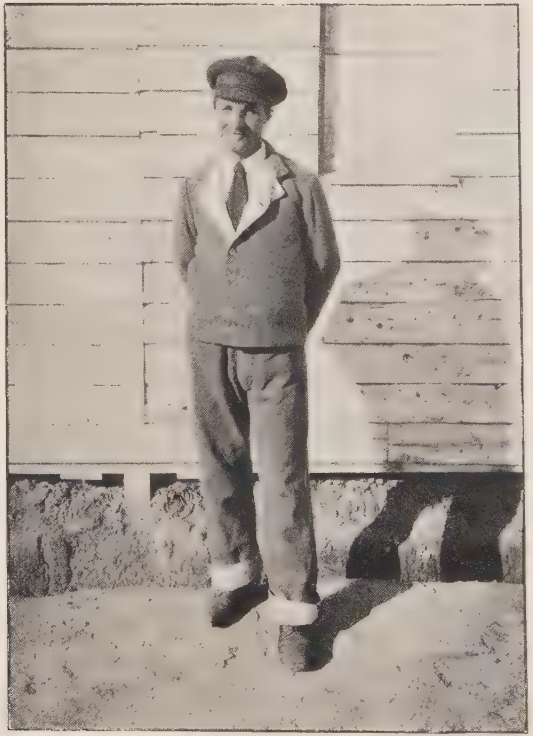
(5) The total amount of quinine received during his stay in hospital should also be noted. He had no relapses, and his appearance in the photograph facing p. 83 shows the tonic effect of quinine in large doses given over a prolonged period.

CASE 7.—*Recovery from Cerebral Malaria.*—Driver S., aged 28. Service, 2 years 10 months. Admitted on October 28, 1917.

*Present History.*—Admitted from — Casualty Clearing Station in a semi-collapsed and semi-comatose condition. Unable to give any particulars of his illness, identity or relatives.



Case 6.—Pioneer R. After recovery from cerebral malaria.
Note this patient's condition at 6 p.m. on October 25, 1917 (p. 80).

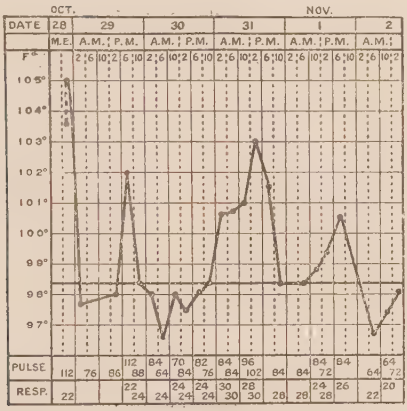


Case 7.—Driver S. After recovery from cerebral malaria.

Face p. 84

*On admission.*—12 noon. Temperature, 105° F.; pulse 112; respirations 22 per minute. Temperature fell to 103·6° F. after intramuscular quinine and sponging. Tongue furred and fairly moist; heart and lungs normal; spleen plus. Nearly comatose, cannot be roused to answer questions.

6.30 p.m. Less drowsy after intravenous quinine.




Case 7. Driver S.

11.30 p.m. Marked improvement in mental condition, and patient is able to give details of his relatives, address, &c. Answers questions fairly rationally after prolonged hesitation. Semi-aphasia and obvious inclination to sleep. General condition good.

*Treatment.*—

Noon. Intramuscular quinine, 20 grains.

6 p.m. Intravenous quinine, 20 grains in saline, 8 ounces.

29/10/17—Temperature subnormal; pulse 76, full and steady; complains of difficulty in speaking.

6 p.m. Temperature, 102° F.; pulse 90; respirations 22.

7.30 p.m. Temperature, 102° F.; pulse 112; rigor lasting for quarter of an hour.

10 p.m. Still drowsy, though quite coherent when spoken to; temperature normal; pulse 98.

12 p.m. Has incontinence of fæces and urine.

*Treatment.*—

10 a.m. Intramuscular quinine, 20 grains.

6 p.m. Intravenous quinine, 20 grains, in saline, 8 ounces.

10 p.m. Intravenous quinine, 20 grains, in saline, 8 ounces.

---

30/10/17—Clearer mentally.

9 a.m. Temperature subnormal; pulse 64; respirations 26; heart sounds clear.

11 a.m. Transferred to intravenous ward; blood film taken; parasite not found, due to the quinine treatment already received.

2 p.m. Speaks quite rationally about kit; pulse full; inclined to be drowsy; this passed off after the intravenous quinine.

6.45 p.m. Passing urine normally; no incontinence now. Urine: no albumin and no sugar.

11 p.m. Better; not restless, but cannot sleep. Morphia, $\frac{1}{4}$ grain hypodermically. Tongue moist and clean.

*Treatment.*—

11.30 a.m. Intramuscular quinine, 20 grains.

2 p.m. Intravenous quinine, 20 grains in saline 8 ounces.

6.40 p.m. Intramuscular quinine, 20 grains.
11 p.m. Quinine sulph., 20 grains, by the mouth.

---

31/10/17—10 a.m. Temperature 101° F.; pulse good; mental condition steadily improving.
5 p.m. Temperature 103° F.; tongue dry.
10 p.m. Temperature normal and tongue more moist.

*Treatment.*—
10 a.m. Intramuscular quinine, 20 grains.
5 p.m. Intramuscular quinine, 20 grains.
10 p.m. Quinine sulph., 20 grains by the mouth.

---

1 11 17—Improving.
11 a.m. Tongue still rather dry.

*Treatment.*—
11 a.m. Intramuscular quinine, 20 grains. Quinine sulph., 15 grains, t.d.s., by mouth, ordered to be continued daily.

---

17/12/17—Discharged to convalescent depôt.

Amount of quinine taken: 1,940 grains in fifty days; daily average, 39 grains. No relapse during this period. In convalescent depot he received quinine 10 grains a day for a month, when he relapsed and was again sent to hospital. His quinine treatment in the depot was, in my opinion, totally inadequate.

*Résumé.*

| | Condition | Treatment |
|---|---|---|
| 28/10/17 | Admitted semi-comatose... | Quinine, 40 grains—one I.M.Q. and one I.V.Q. |
| 29/10/17 | a.m. Aphasia<br>10 p.m. Still drowsy | Quinine, 60 grains—one I.M.Q. and two I.V.Qs. |
| 30/10/17 | a.m. Drowsy<br>11 p.m. Mental condition improving | Quinine, 80 grains in 12 hours—two I.M.Qs., one I.V.Q. and oral quinine (20 grains). |
| 31/10/17 | Further improvement in mental condition | Quinine, 60 grains—two I.M.Qs. and one oral quinine (20 grains). |
| 1/11/17 | Improving. Tongue still rather dry | Quinine, 65 grains—one I.M.Q. (20 grains), and the rest by mouth. |
| 2/11/17 | Mental condition good ... | Quinine, 45 grains daily. |

*Personal statement* of Driver S. after recovery from cerebral malaria.

"I remember having two bad days with my unit during which time I at times *lost my vision* and also was unable to stand on my feet. Doctor having sent me to hospital, I remember being in the field ambulance, then being placed upon a stretcher in a motor for a clearing station. I remember just before leaving the casualty clearing station for the train, some of my kit was short which was wrapped in a waterproof sheet. Just about this time, *my speech was beginning to fail me.* I remember having a rigor on the train. I remember being taken out of the train to a hospital and carried on a stretcher to a ward door. After that I can remember nothing at all until an orderly bathed me. I then remember having another rigor and an intravenous into my arm by Captain Alport and another doctor. *After that I tried to speak, but could not.* I knew I was very ill, and at one time opened my eyes and found somebody examining my chest. I remember quietening down after the intravenous and the next thing I remember was waking up and finding myself in a strange ward. I remember having another intravenous. After that, was muddled, and the next thing I remember was the Jewish Chaplain coming in and telling me he had seen me a week before, but I don't remember having seen him before. I remember at this time I had an idea in my head that the war was over. After that I can remember fairly well." "A. S.

"Witnesses:

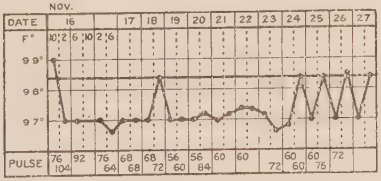
"T. W. ARNISON,
"*Lieutenant, R.A.M.C.*
"W. L. ANDREWS,
"*Sister (T.F.N.S.).*
"*— General Hospital,*
"*December* 14, 1917."

*Comments.*—(1) Patient was not vigorously enough treated in the early stages for which reason it took six days for his mental condition to return to normal. The rigor on October 29, 1917, also proves this to be the case.

(2) Unfortunately, parasites were not found in the blood film, but the fact that he relapsed in the convalescent depot after the vigorous treatment he received in this hospital, makes it highly probable that the malignant tertian parasite was the cause.

CASE 8. *Recovery from Cerebral Malaria.*—Driver D., aged 31. Service, 2 years 3 months. Admitted on November 16, 1917. In Balkans, 1 year 2 months.

*Previous history.*—Unconscious on admission. History obtained on November 18, 1917. Malaria in August, 1917. Frequent mild attacks since.




Case 8. Driver D.

Onset of present illness, November 14, 1917.

*Symptoms.*—Headache, pains in back and legs. Shivering, sweating, no vomiting.

*On admission.*—Admitted at 10.30 a.m. in an unconscious condition, rambling a little. No response to questions. No swallowing. Reflexes normal. Anæmic. Spleen plus. Some response to prick of needle when giving intramuscular quinine.

11.30 a.m. Patient again responded to stimulus of needle when receiving the intravenous quinine. Food given; not swallowed but retained in throat and returned. Patient spoke a few words. Appears mentally unbalanced, and had a fit of sobbing.

1.30 p.m. Patient unconscious; not swallowing; not taking notice; eyes staring. Remained like this until 3·45 p.m., but during this time occasionally moved hand and turned head towards it; sometimes put hand to head. Colour bad. Pulse 84, very feeble. These improved a little, and at 3·45 p.m. sudden improvement in mental condition as well, after his quinine. Patient spoke quite rationally and answered a question. Vomited once, and expressed a desire to urinate, and passed water. Put out tongue on request; tongue moist and slightly furred. Took nourishment by mouth.

6 p.m. Patient improving; pulse a little better.
*Blood film:* malignant tertian, crescents.

*Treatment.*—

10.35 a.m. Intramuscular quinine, 20 grains; rectal saline 10 ounces.

11.30 a.m. Intravenous quinine, 30 grains in saline 8 ounces.

1.30 p.m. Strychnine, $\frac{1}{30}$ grain; rectal saline, 10 ounces with brandy.

3.30 p.m. Intramuscular quinine, 20 grains.

6 p.m. Quinine, 15 grains, by mouth.

CASE 8.—Driver D. After recovery from cerebral malaria.

Well-marked Kernig's sign in cerebrospinal meningitis. CASE 9.—Lance-Corporal A. (See p. 95.)

17/11/17—Patient better; mental condition normal. Evening: improved, but inclined to be talkative and a little hysterical.

*Treatment.*—

Quinine sulph., 20 grains, t.d.s.; evening, pot. brom., 20 grains.

18/11/17—Much better, but still hysterical.

*Treatment.*—Intramuscular quinine, 20 grains; quinine, 15 grains, t.d.s., by mouth, to be continued daily.

Driver D. received quinine, 1,330 grains in thirty-one days; average, 43 grains a day.

*Personal statement* of Driver D., after recovery from Cerebral Malaria.—"I remember going into the camp hospital and being unable to carry my kit to the ambulance. I remember being laid on a seat in the ambulance and being in a 'staring' condition. I then remember nothing until I saw a doctor putting a needle into my arm (for the intravenous), *but I could not speak*. I remember shortly after that Sister said she was going to give me some food, and then I can remember nothing until I saw a gentleman coming in and taking a photo of a man's leg next to me. I remember writing a letter two days after I came to my senses, and that the date of the letter was 22nd November, 1917. After this, I can remember practically everything.

"W. D.

"Witnesses:

"T. W. ARNISON,

"*Lieutenant, R.A.M.C.*

"W. L. ANDREWS,

"*Sister (T.F.N.S.).*

"— *General Hospital,*

"*December* 14, 1917."

*Résumé.*

*Blood film:* Malignant tertian crescents and increased mononuclears.

| | Condition | Treatment |
|---|---|---|
| 16/11/17— | | |
| 10 a.m. | Admitted unconscious; no response to questions; no swallowing | Quinine, 70 grains in five hours—one I.V.Q. (30 grains) and two I.M.Qs. (40 grains); also 15 grains by the mouth later |
| 3.45 p.m. | Sudden improvement; spoke quite rationally | |
| 17/11/17—Very | talkative; tongue cleaner and more moist | Quinine, 15 grains, t.d.s. |
| 18/11/17—Still | verbose ... ... | Quinine, 65 grains — one I.M.Q. 20 grains and the rest by the mouth |
| 19/11/17—Mentally | normal ... ... | Quinine, 45 grains continued daily |

A comparison of this case with the next is of the utmost importance, as it brings out very convincingly the value of quinine in the differential diagnosis between cerebral malaria and cerebrospinal meningitis.

CASE 9. *Death from Cerebrospinal Meningitis.*—Lance-Corporal A., aged 37. Service, 2 years 3 months. Admitted November 15, 1917.

*Present history.*—Complained of headache.

*On admission.*—Severe headache.

7 p.m. Became unconscious, transferred to the cerebral ward.

8 p.m. In state of coma, varying a little in depth from time to time; spleen palpable; conjunctival and corneal reflexes present; pupils contracted and equal, do not react to light; was roused by prick of needle sufficient to struggle when intramuscular quinine was given.

9 p.m. No response to needle with intravenous quinine injection; coma, deep; respirations occasionally Cheyne-Stokes in character; pulse good.

11 p.m. Struggled very much when given intramuscular quinine; reflexes, brisk; pupils more dilated and reacting; restless.

*Treatment.*—

8 p.m. Intramuscular quinine, 20 grains.

9 p.m. Intravenous quinine, 30 grains, in saline, 10 ounces.

11 p.m. Intramuscular quinine, 20 grains.

16/11/17—6.30 a.m. Made request to urinate and did so.

9 a.m. Mental state appears more active; enema given, and he asked for bed-pan; very difficult to persuade him to do anything; drowsy when saline was given and more so afterwards.

11 a.m. *Report on blood film:* Polymorphonuclear leucocytosis; parasites not found.

12.30 p.m. Still drowsy, responds to attempts to rouse him by opening eyes and nods head sometimes in reply to a question.

1.30 p.m. Very drowsy, no response to questions. Breathing quiet, no stertor, no Cheyne-Stokes.

1.45 p.m. Roused sufficiently to speak and pass water.

2.30 p.m. Spoke and said he was "a bit better."

3.15 p.m. Put out his tongue on request; tongue dry and furred.

5.45 p.m. Some stiffening of muscles of back of neck, slight retraction of head; thighs and legs flexed; well-marked Kernig's sign—when eliciting this the pain roused the patient; plantars active and flexor.

6.25 p.m. Lumbar puncture, turbid fluid under considerable pressure. After this he appeared to be less drowsy but complained of headache.

*Treatment.*—

9 a.m. Intravenous quinine, 30 grains, in saline, 8 ounces.

3.30 p.m. Intramuscular quinine, 20 grains.

*Report on Cerebrospinal Fluid.* — Polymorphonuclear leucocytosis and meningococci present.

Patient was transferred to hospital for cerebrospinal meningitis on November 17, 1917 and died December 3, 1917.

*Résumé*

*Blood film:* Polymorphonuclears but no parasites found.

| | Condition | Treatment |
|---|---|---|
| 15/11/17 | Coma, varying in depth | Quinine, 70 grains, in three hours —one I.V.Q. (30 grains) and two I.M.Qs. |
| 16/11/17 | Still comatose ; no improvement to speak of | Quinine, 50 grains — one I.V.Q. (30 grains) and one I.M.Q. |

*Comparison with Driver D.'s Case* (No. 8).

| | Driver D. | Lance-Corporal A. |
|---|---|---|
| 1. | Admitted on October 16, 1917. | Admitted on October 15, 1917. |
| 2. | Blood film : malignant tertian parasites and relative mononuclear increase. | Polymorphonuclear leucocytosis. |
| 3. | Comatose condition cleared up rapidly on receiving quinine, 70 grains in five hours—intravenously and intramuscularly. | Comatose condition scarcely improved after quinine, 70 grains in three hours, by the same methods. |

*Comments.*—These two men were lying opposite one another in the same ward.

Finding that one patient yielded rapidly to quinine

treatment while the other did not, it was necessary to discover the reason without delay. The results of the blood slides threw light on the subject.

Lance-Corporal A.'s film showed marked polymorphonuclear increase. As there was nothing to account for this in the chest or abdomen, lumbar puncture was clearly indicated. This, apart from Kernig's sign and retraction of the head, clinched the diagnosis.

Kernig's sign was very well marked just before the patient was transferred early the following morning. A photograph of this will be found facing p. 91.

(2) Compare also, the lumbar puncture results in this case with that of Case No. 4. Private R. (p. 71), who died of cerebral malaria.

| *Cerebral Malaria.* | *Cerebrospinal Meningitis.* |
|---|---|
| Cerebrospinal fluid; clear, not under pressure. Bacteriological report: Fluid clear, sterile, six cells per cubic millimetre. | Fluid; turbid, and under considerable pressure. Bacteriological report: Polymorphonuclear leucocytosis, meningococci present. |

CASE 10. *Recovery from Cerebral Malaria.*—Sergeant C., aged 44. Service, 3 years 4 months. Admitted October 23, 1917. In Balkans, 1 year 10 months.

*Previous history.*—Shivers.

*Onset of present illness.*—October 18, 1917.

*Symptoms.*—Shivering, sweating, no vomiting; pains all over, especially in back.

*On admission.*—Temperature, 102·8°F.; pulse 84; tongue, white, furred; heart, mitral systolic transmitted; lungs, nil.; spleen, palpable, marked tenderness.

*Blood film:* Malignant tertian rings.

*Treatment.*—Calomel and mist. alb.; quinine sulph. 15 grains, t.d.s., to be continued daily.

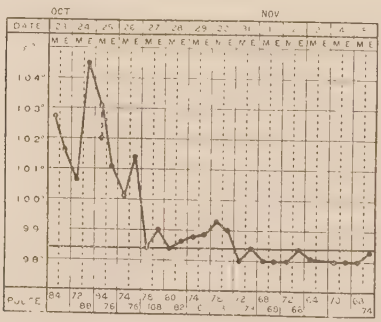
*Progress.*

24/10/17—Temperature, 104·6°F.; intramuscular quinine 15 grains.

25/10/17—Patient worse; intramuscular quinine 20 grains; brandy 1 ounce, 4-hourly.

26/10/17—10 a.m. Speech difficult, cannot find the proper word; very excitable; muscles twitching; pulse weak.

2.30 p.m. Intravenous quinine 20 grains in saline, 8 ounces.




Case 10. Sergeant C.

9 p.m. Highly excited; pulse full and bounding; intramuscular quinine 40 grains, morphia ½ grain hypodermically, pot. brom. 20 grains, repeated in four hours.

27/10/17—3 p.m. Seizure, could not speak for half an hour; could not be roused; left leg extended and fixed; right side twitching, this lasted about an hour.

*Treatment.*—

Noon. Intramuscular quinine 20 grains.

5 p.m. Intravenous quinine, 20 grains, in saline, 8 ounces.

10 p.m. Intravenous quinine, 20 grains, in saline, 8 ounces.

---

28/10/17—Mental condition brighter, able to speak; pupils react to light and accommodation, knee jerks normal; ankle clonus present; no deviation of tongue; voluntary efforts cause twitching.

*Treatment.*—

10.45 a.m. Intramuscular quinine 30 grains.

9.30 p.m. Intravenous quinine, 20 grains, in saline 8 ounces, quinine sulph. 45 grains, still continued daily.

---

29/10/17—Mental condition much clearer; slept fairly well; tongue cleaner; muscular twitching not so marked.

11 a.m. *Notes by Colonel Purves Stewart, Consulting Physician to the Forces*: — "Patient slightly confused but speaks clearly without aphasia; occasionally coarse tremors of head, neck and limbs at all joints, chiefly on voluntary movement; on attempting to grasp objects keeps alternately clenching and releasing grasp of fingers. Pupils and cranial nerves normal; no cutaneous anæsthesia or analgesia; all voluntary movements are coarsely tremulous, but no paralysis of any limb, supinator-jerks, knee-jerks and ankle-jerks present; no true ankle

clonus; planter reflexes feeble; abdominals present and equal; spleen no longer palpable; soft, systolic bruit at apex."

3 p.m. Intramuscular quinine 30 grains.

11 p.m. Intramuscular quinine 30 grains.

30/10/17—Twitching not so severe; mental condition improving; voluntary movement still tremulous.

*Treatment*—6 p.m. Intramuscular quinine 30 grains.

31/10/17—Quinine sulph. 15 grains, t.d.s., by mouth, still continued.

1/11/17—Tremor still present, making speech difficult; intelligent, and talks about the war.

4/11/17—Tremor not so coarse, and much less.

8/11/17—Still some difficulty with words especially if he gets excited.

17/11/17—Grasp still tremulous, but has been able to feed himself for last two days; mentally alert; pulse normal, 72.

20/11/17—"Up" to-day.

23/11/17—Out of doors for two hours—sitting in chair.

30/11/17—Still very weak; tremors decreasing.

*Treatment.*—Quinine sulph. reduced to 10 grains, t.d.s.

7/12/17—Stronger, but cannot walk without assistance; knee-jerks slightly exaggerated.

18/12/17—Great improvement, putting on flesh; nervousness almost gone; no tremor of tongue; volitional tremor very much less.

*Treatment.*—Liq. strych., 5 minims, t.d.s.

28/12/17—Quinine sulph. increased to 15 grains, t.d.s.

31/12/17—Walked round ward without assistance; somewhat shaky; very fine tremor of outstretched hands.

8/1/18—Left by Hospital Ship for England.

Cerebral malaria cases. After recovery. CASE 10.—Sergeant C. in bed.

Three patients after recovery from cerebral malaria. Photo taken during an air raid while shrapnel was falling in the hospital grounds.

*Résumé of daily Quinine Treatment.*

| | Orally | Intra-muscularly | Intra-venously | Total |
|---|---|---|---|---|
| 23/10/17 | 45 grains | ... | ... | 45 grains |
| 24/10/17 | 45 „ | 15 grains | ... | 60 „ |
| 25/10/17 | 45 „ | 20 „ | ... | 65 „ |
| 26/10/17 | 45 „ | 40 „ | 20 grains | 105 „ |
| 27/10/17 | 45 „ | 20 „ | 40 „ | 105 „ |
| 28/10/17 | 45 „ | 30 „ | 20 „ | 95 „ |
| 29/10/17 | 45 „ | 60 „ | ... | 105 „ |
| 30/10/17 | 45 „ | 30 „ | ... | 75 „ |

1/11/17 to 30/11/17—45 grains a day ... 30 days
1/12/17 to 28/12/17—30 grains a day ... 28 „
29/12/17 to 8/1/18—45 grains a day ... 10 „

Total amount of quinine taken = 3,295 grains in 77 days.

| Orally | Intramuscularly | Intravenously |
|---|---|---|
| 3,000 grains | 215 grains | 80 grains |

*Daily average* ... ... ... ... ... 43 grains
During acute stage (26/10/17 to 30/10/17)... 485 „
Daily average for these five days ... ... 97 „

*Comments.*—(1) The mental condition, difficulty in speaking, the seizure, and the muscular twitchings are in striking contrast to the coma in the other cerebral cases.

(2) The enormous quantity of quinine this patient took and the way he progressively improved on it should be borne in mind.

In the foregoing series, I have dealt fully with three deaths and six cases of recovery from cerebral malaria, and I think I have advanced fairly strong arguments for the method and dosages I use.

I possess full notes on the condition and treatment of a considerable number of other patients who recovered after attacks of the above disease. These are of great

interest, and I hope to be able to give them in an enlarged edition of this work at some future date.

Appended is a scale of quinine dosage for guidance in the treatment of all cases of cerebral malaria.

I again repeat that the method of administration and the doses are absolutely safe, are of the greatest value in differential diagnosis, and, in my experience, have never failed to secure satisfactory results.

### Scale of Doses in Cerebral Malarial Patients.

Quinine 20 grains in each dose in each case. Each injection should be 20 grains of quinine bihydrochloride unless otherwise stated.

*On admission.*

| | |
|---|---|
| (1) In early cases showing symptoms of drowsiness, aphasia, nervous twitchings, tendency to get out of bed, &c. | Quinine 60 to 80 grains in twelve hours; two intravenous and one or two intramuscular injections |
| (2) In semi-comatose and delirious cases | Quinine 80 to 100 grains in twelve hours; an initial dose of 30 grains in normal saline, 8 ounces, with 20 grains intramuscularly, followed later by an intravenous and another intramuscular |
| (3) In comatose cases ... | Quinine 100 to 120 grains in twelve hours; an initial dose of 40 grains in 8 ounces of normal saline, with 20 grains intramuscularly, followed by an intravenous and an intra- |

muscular, and later by a further intravenous or intramuscular injection—both if necessary

*After-treatment.* — On second day, two intravenous injections and one intramuscular.

On third day, one intravenous and two intramuscular. On the days following, give intravenous, intramuscular or injections per rectum as required.

The after-treatment of course depends upon the progress made. As soon as the patient is mentally clear, and his other nervous symptoms have disappeared, all injections should be stopped, and quinine 15 grains t.d.s. by the mouth commenced. It should be remembered, however, that it is useless to start oral quinine unless :—

(*a*) His bowels are acting well.

(*b*) His tongue is clean and moist.

The underlying principle of this "large dose intravenous and intramuscular" method of treatment, is to make an immediate and direct attack on the parasite in the blood by means of the intravenous, and to continue the effect by means of the intramuscular injection, which is slowly absorbed over a period of from one to twelve hours.

## CHAPTER VI.

## PERNICIOUS MALARIA WITH CARDIAC SYMPTOMS AND COLLAPSE.

THIS is one of the most serious conditions with which the medical officer has to deal. Prompt quinine treatment by the intravenous route combined with cardiac stimulants are required.

*Causation.*—(1) The effects of the toxins of malaria on the heart muscle; (2) insufficient administration of quinine.

CASE 1.—Pte. F., aged 23. Service, two years. Diagnosis: Malignant malaria. Admitted on September 16, 1917. In Balkans, eight months.

*Previous history.*—No malaria.

*Onset of present illness.*—September 9, 1917.

*Symptoms.*—Headache, backache, rigors, sweating, vomiting.

*On admission.*—Temperature normal, pulse 80; tongue clean; heart and lungs normal; spleen plus and tender.

*Blood film.*—Malignant parasites.

*Treatment.*—Quinine 15 grains, t.d.s., to be continued daily.

---

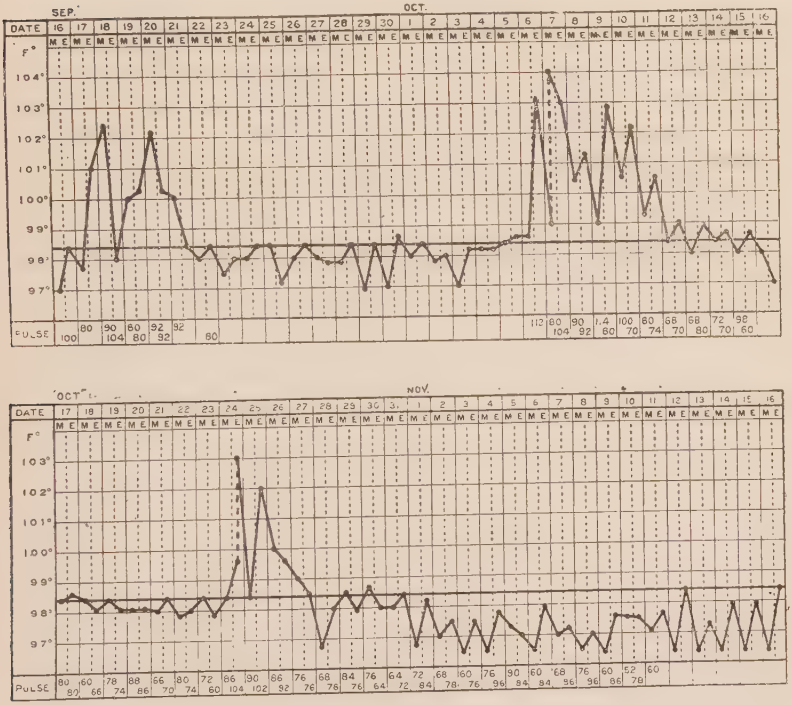
18/9/17—Temperature rose to 102° F., pulse 90.
19/9/17—Temperature and pulse normal.
20/9/17—Temperature again rose to 102° F., pulse 92.
21/9/17—Temperature fell to normal and remained so until 6/10/17.

24/9/17—Quinine reduced to 30 grains daily.

1/10/17—Patient very anæmic; complains of pain over the spleen.

6/10/17—Sudden rise of temperature to 103° F., pulse 112.

7/10/17—Temperature 104° F., pulse 104. Quinine increased to 40 grains, daily.




Case 1. Private F.

8/10/17—Temperature 101° F., pulse 92.

9/10/17—Temperature 102° F., pulse 80.

10/10/17—Temperature 102° F. Patient suddenly collapsed; lips and skin pallid; pulse thready, almost imperceptible at wrist.

*Treatment.*—

10 a.m. Intravenous quinine 10 grains, with brandy 2 ounces in normal saline 8 ounces; quinine 15 grains, t.d.s., by mouth as before; strychnine $\frac{1}{60}$ grain and digitaline $\frac{1}{100}$ grain hypodermically 4-hourly.

8.30 p.m. Intravenous quinine 10 grains in 8 ounces of saline.

---

12/10/17—Temperature normal, pulse 70. Patient very pallid and anæmic looking. Temperature remained normal until 24/10/17.

14/10/17—Mist. arsen. tonic, graduated doses, continued until 25/10/17.

20/10/17—Quinine again reduced to 30 grains a day.

24/10/17—Temperature once more rose to 103° F., pulse 104. Quinine increased to 45 grains a day.

25/10/17—Temperature 102° F., pulse 102.

26/10/17—Temperature 100° F., pulse 99. Patient collapsed for second time; heart sounds almost inaudible; pulse flickering, very soft; great pallor.

*Treatment.*—

11 a.m. Intravenous quinine, 20 grains, in saline 8 ounces.

6 p.m. Intravenous quinine, 20 grains, in saline 8 ounces. Brandy 4-hourly.

---

27/10/17—Patient much improved.

31/10/17—Steady improvement.

*Treatment.*—Tab. iron and arsen., t.d.s. p.c., as well as the quinine 15 grains, t.d.s., by mouth.

6/11/17—Still weak and anæmic.

*Treatment.*—A second course of mist. arsen. tonic, graduated doses, commenced.

---

5/1/18—Patient perfectly fit; no anæmia; no collapse or relapse since November 24 last.

Left hospital for embarkation to England.

*Comments.*—This man was admitted on September 16, 1917. At that time the necessity for early and vigorous treatment by quinine was not fully understood by us.

He came in with a normal temperature, and was very rightly put on to quinine 15 grains t.d.s.

Two days later, his temperature rose to 102° F., and again on September 20, 1917—quite typical but unnecessary. He should have had an intramuscular quinine 20 grains on each of these days.

On September 24 the medical officer reduced the quinine to 30 grains a day, and puts it on record that on October 1, patient complained of pain over the spleen and that he was very anæmic.

On October 6, patient relapsed, and notwithstanding an increase of quinine 45 grains a day, there was a considerable daily rise of temperature for the next four days. No effort appears to have been made to cope with these rises either by intramuscular, intravenous or rectal injections.

In due course, October 10, patient collapsed and intravenous quinine and stimulants had to be resorted to.

After this the temperature remained normal, and the quinine, on October 20, was reduced to 30 grains a day. This amount not being enough to prevent the formation of the toxins in the blood, the temperature, four days later, once more rose to 103° F. It remained up on

October 25 and 26, when a second collapse took place, and we had to fall back on intravenous quinine injections.

Again, no intramusculars had been given. Merely increasing the daily issue of quinine to 45 grains in the case of a man with a high continued temperature who, in all probability, was absorbing very little by the mouth, was a short-sighted policy.

The treatment after this collapse: Quinine 45 grains by mouth daily, with graduated doses of iron and arsenic, was excellent, and the ultimate result, as the notes show, was all that could be desired.

Case 2. *Death from Cardiac Failure in Malignant Malaria.*—Sergeant H., aged 45. Service, 3 years. Admitted November 29, 1917. In Balkans, 2 years 1 month.

*Previous History.*—Possible attack of malaria in the summer of 1916, mild fever.

*Onset of present illness.*—Six days ago (November 23, 1917).

*Symptoms.*—Headache, pain over eyes, general malaise, cold feeling; no definite rigor until three days later. Reported sick two days ago. Diagnosed as malaria by the Regimental Medical Officer and given quinine.

*On admission.*—Temperature 104° F.; conjunctivæ, slight icteric tinge; tongue, fairly clean; spleen, tender but not palpable; heart sounds rather feeble, no bruits heard; pulse, soft, rapid, but steady; lungs, a few râles at both bases.

*Blood film.*—Malignant tertian; trophozoites and gametocytes; numerous ring forms.

*Treatment.*—Quinine 15 grains, t.d.s.

*Progress.*—30/11/17. Temperature normal; pulse 90 per minute, steady.

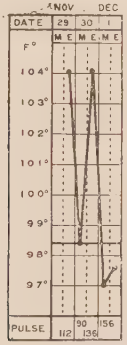
6 p.m. Temperature 104° F.; vomited. Intramuscular quinine 20 grains given.

11.30 p.m. Patient bad, temperature still up. Intramuscular quinine 20 grains given.

1/12/17—4.30 a.m. Patient very collapsed after retching for ten minutes. No pulse felt at wrist. Officer in command of Medical Division called in. Intravenous quinine saline ordered.

*Treatment.*—

5 a.m. Subcutaneous saline 10 ounces with 10 grains of quinine into left axilla, after failure at veins; pituitrin 1 cubic centimetre.




Case 2. Sergeant H.

9.30 a.m. Slightly better; pulse countable, 156; temperature subnormal; quite clear mentally; no more vomiting.

*Treatment.*—Brandy 1 ounce every four hours; strychnine $\frac{1}{60}$ and digitaline $\frac{1}{100}$ grain 4-hourly.

2.30 p.m. Temperature subnormal; condition about the same; transferred to intravenous ward; patient dying.

4 p.m. Intravenous quinine 20 grains in 8 ounces of saline given. When about 5 ounces had

been injected, patient appeared worse; pulse imperceptible at wrist; pituitrin 1 cubic centimetre given; pulse improved again before the end of the injection, and patient was less collapsed and warmer. A few minutes later some twitching of face on both sides, and contraction of flexors of arms and legs.

4.30 p.m. Patient losing consciousness; reflexes brisk; pulse better; rectal saline 10 ounces with brandy.

6 p.m. Still unconscious; pulse weaker; perspiring freely; respirations assuming Cheyne-Stokes character; strychnine $\frac{1}{30}$ grain given hypodermically, and oxygen inhalations tried.

7.40 p.m. Patient died.

*Post-mortem report.*—Brain: Slight amount of œdema and injection of both membranes and substance.

Heart: Dilated. Muscle extremely pale and atrophic. Valves normal.

Liver: Enlarged, pale and bile-stained.

Spleen: Three times normal size, very soft and diffluent, indeed semi-fluid, very dark in colour.

Kidneys: Left, much enlarged, and contained in its pelvis three large masses of phosphatic calculi with branches projecting into the calices. Right kidney normal.

Other organs normal.

*Comments.*—(1) There is no record that this man had any quinine until seen by the regimental medical officer two days before admission. He then probably received 20 or 30 grains a day. When admitted here, he was put on to 45 grains by mouth. The next day, he got two

intramusculars of 20 grains each, as well as quinine by the mouth, and on the last day an intravenous of 20 grains.

(2) On account of his age (45 years) and the state of his heart and other organs, it is difficult to say whether if I had seen him eighteen hours earlier, and had given him large doses of quinine intravenously and intramuscularly, he would have recovered. I think it is quite possible. (See bottom of page 36.)

(3) The fact that the medical officer in charge of the case failed with the first intravenous injection was unfortunate.

(4) The bacteriological report on the blood slide—trophozoites and gametocytes, numerous ring forms—was an indication for a speedy introduction of quinine into the circulation in sufficient quantities (100 grains in twelve hours).

CASE 3.—Private D., aged 54. Diagnosis : Malaria recurrent. Admitted September 20, 1917. Died September 21, 1917. Cause of death : heart failure. Had malaria previously.

NOTE.—This patient collapsed suddenly on the day after admission, and died almost immediately.

*Post-mortem report.*—Brain : No macroscopic change.

Heart: Soft and dilated; inflammation of aortic cusps; heart muscle very fatty, and chambers dilated.

Spleen : Much enlarged, very soft and diffluent.

Liver: Slightly enlarged and congested.

Kidneys : Congested.

CASE 4.—Driver F., aged 25. Diagnosis : Malaria and dysentery. Admitted August 31, 1917. Died October 11, 1917. Cause of death : heart failure.

*History.*—Three times in hospital with malaria.

*Blood film.*—Malignant tertian positive.

*Report on Stools.*—No Shiga, Flexner or "Y" organisms found.

NOTE.—This patient collapsed, and died suddenly while in the act of swatting a fly.

*Post-mortem report.*—Brain: Substance showed a considerable number of petechiæ and punctate areas of necrosis.

Heart: Muscle extremely soft and thin; cavities dilated.

Lungs: Congestion of bases and some bronchitis.

Spleen: More than double the normal size. Very soft, dark and friable.

Liver: Large, dark and pigmented.

Intestines: In the ascending colon near the hepatic flexure, several areas of congestion, hæmorrhage and superficial necrosis.

Kidneys: Markedly congested.

## EFFECT OF THE MALARIA PARASITES AND TOXINS ON THE HEART.

A study of the post-mortem reports given in this book shows that the heart is soft, generally fatty, always thin-walled, and the cavities dilated. The valves are normal as a rule. Factors which tend to weaken the heart in malaria are:—

(1) *Age.*—Men over forty years of age are more liable to have the heart and other organs damaged by the malarial poisons than the younger men who have a greater power of resistance.

(2) *Relapses.*—During an acute attack of malaria of any kind it is quite common to find a mitral systolic bruit, and an accentuated second sound in the pulmonary area. Following a primary attack of malaria the pulse and the heart sounds become normal again. After one or two relapses, you may have bradycardia or a mild tachycardia,

but as the relapses succeed each other, tachycardia and other irregularities of the heart become more marked.

The damage to the heart, brain, spleen, kidneys and other organs is, to my mind, the strongest possible argument in favour of early, and where necessary, prolonged treatment with large doses of quinine. By this means the brain clears up, tachycardia disappears, splenic enlargement and tenderness subside, and the other organs become normal.

Later on I shall deal with quinine combined with arsenic and galyl and their effect on post-malarial anæmias, &c.

## Other Forms of Pernicious Malaria.

### (1) *Acute Hæmorrhagic Pancreatitis.*

Case 1.—Sergeant L., aged 38. Service 5 years. Admitted on September 11, 1917, at 12.30 p.m.

*Previous history.*—Indefinite period of indigestion with constipation.

*Onset of present illness,*—Yesterday, took a dose of castor oil. When the bowels began to act he was seized with sudden acute pain "in the stomach." Felt sick, but brought nothing up; bowels acted slightly.

*On admission.*—Complained of pain in the left hypochondrium; very collapsed. He looked ill, and was groaning with pain; temperature 97·6° F.; pulse 120; respiration 32; heart normal; chest: a few bronchitic sounds; abdomen, left rectus muscle rigid; right rectus less so; no circumscribed area of pain; shifting dulness in epigastrium, from side to side; would persist in lying on his right side with knees drawn up.

*Operation.*—1.30 p.m. Laparotomy in mid-line above umbilicus; abdominal cavity full of blood and clot; liver, large and soft; posterior peritoneal sac explored;

no evidence of visceral lesion except pancreas; blood was welling up from the foramen of Winslow; the pancreas was hard and nodular to the touch, and showed marked congestion and hæmorrhage. Two large drainage tubes were inserted and the abdominal wall sutured; two pints of saline were injected subcutaneously during the operation; patient very collapsed, and pulse weak and thready.

*In Ward.*—Saline per rectum, with brandy 1 ounce to the pint, given at intervals.

Case 1. Sergeaut L.

September 12, 1917. — Retained rectal salines, and passed a fair night. Died at 1.15 p.m.

*Post-mortem report.* — Early post-mortem staining. Large hæmorrhages into the peritoneal cavity.

Liver: Very enlarged.

Spleen: Very enlarged and diffluent; no perisplenic adhesions or capsule thickening.

Kidneys: Enlarged.

Suprarenals: Show acute hæmorrhage into their substance.

Pancreas: Multiple hæmorrhages and much œdema, salmon-pink tint; large peripancreatic hæmorrhage; peritoneal cavity free from any peritonitis; viscera contracted.

Heart: Enlarged.

Lungs, brain, thyroid gland and pituitary gland, normal.

*Report by Base Laboratory.*—"Liver: No fatty changes. Malarial pigment abundant. No evidence of fat necrosis on naked eye or microscopical examination of the various tissues sent here."

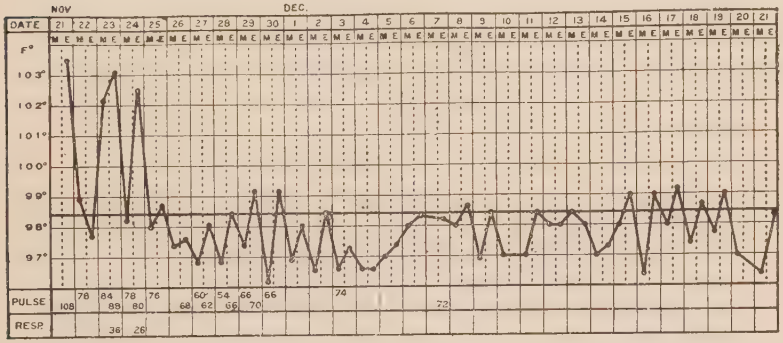
### (2) *Types showing Great Blood Destruction.*

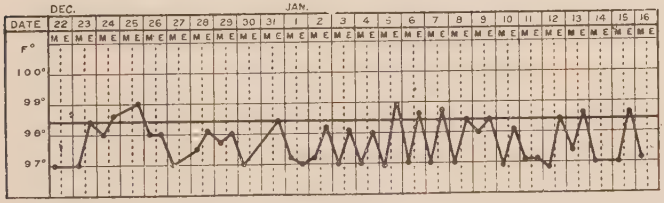
Case 2. *Malaria, Recurrent, with Jaundice.*—Private N., aged 19. Service, 2 years. Admitted on November 21, 1917. In Balkans, 1 year 2 months.

*Onset of present illness.*—Two days ago.

*Symptoms.*—Headache and shivering; no vomiting.

*On admission.*—Temperature 103·4° F.; pulse, regular, thready; patient very exhausted; headache; jaundice very marked all over; tongue, dry, white; heart, apex




Case 2. Private N.

beat diffuse; spleen, plus and tender; abdomen, tender all over; liver, enlarged and tender.

*First blood film:* Negative.

*Treatment.*—Quinine 15 grains, t.d.s.

---

22/11/17.—Temperature normal; pulse improved; bowels moved; tongue moist and clean.

23/11/17—9 a.m. Temperature 102° F.; no mental symptoms.

5 p.m. Temperature 103° F.; pulse 86, regular; respirations 36; spleen much enlarged, hard and tender; liver enlarged.

*Treatment.*—Quinine sulph. 15 grains as usual.

9 a.m. Intramuscular quinine 20 grains.

5 p.m. Intramuscular quinine 20 grains.

---

24/11/17—9 a.m. Temperature normal; jaundice less marked.

*Second blood film:* Malaria parasites (type undetermined), young trophozoites.

4 p.m. Temperature 102·6° F.; pulse 80, good volume; respirations 26; slight sweating during afternoon; no vomiting; taking quinine well by mouth; slight deafness.

*Treatment.*—Quinine 20 grains, t.d.s., by mouth.

---

25/11/17 Temperature normal; pulse good; quinine 60 grains a day, continued.

26/11/17 Progress satisfactory; temperature normal; tongue clean; slightly deaf.

*Treatment.*—Quinine reduced to 15 grains, t.d.s., daily.

---

29/11/17. Jaundice disappearing; spleen palpable, not tender.

4/12/17. Slight jaundice only; mist. arsen. tonic (increasing doses).

21/12/17. Mist. arsen. tonic stopped; complained of pains in abdomen.

24/12/17. Further reduction of quinine to 30 grains daily.

27/12/17. No jaundice; tongue clean; second course of mist. arsen. tonic commenced.

16/1/18. No relapses; not anæmic; feeling fit; discharged to convalescent depot.

*Comments on N.'s Case* — (1) Patient was extremely jaundiced on admission ; spleen and liver enlarged and tender, but no bilious vomiting.

(2) Condition cleared up on doses of quinine averaging 60 grains daily for the first five days, followed by 45 grains a day for a month, and then 10 grains t.d.s. for another three weeks.

(3) Two courses of arsenic in graduated doses were also of great assistance, in overcoming the anæmia.

---

### (3) *Bilious Remittent Fever.*

A disease characterised by enlargement of the liver, jaundice, bilious vomiting, bile-stained urine and either bilious diarrhœa or constipation ; hiccough may or may not be a symptom. The excessive bile production is due to a great destruction of the red blood corpuscles by the malaria parasite. The temperature is only remittent in cases not properly treated. Efficient quinine treatment reduces it to the ordinary intermittent type of malarial fever.

CASE 3. *Death from bilious remittent fever with cerebral complications.*—Private P., aged 35. Service, 6 months. Admitted on September 29, 1917. Never had malaria before.

*Onset of present illness.*—September 25, 1917.

*Symptoms.*—Headache, shivering, sweating, pain in back, vomited twice, constipated.

*On admission.*—Temperature 102·4° F. ; pulse 136 per minute ; conjunctivæ, icteric tinge ; skin jaundiced ; tongue dry, brown fur ; heart and lungs normal ; spleen plus but not tender ; tenderness over cæcum.

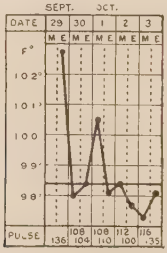
*Treatment.*—Calomel 5 grains, mist. alb. 1 ounce, mane, intramuscular quinine 20 grains.

*Progress.*—September 30, 1917. No improvement.
*Treatment.*—Quinine 15 grains, t.d.s., by mouth.

---

1/10/17—2 a.m. Pulse poor, strychnine $\frac{1}{60}$ grain, digitaline $\frac{1}{100}$ grain, hypodermically; hiccough troublesome; tinct. iodine 2 minims.

4.30 a.m. Slight improvement in pulse, and hiccough has stopped.




Case 3. Private P.

9.30 a.m. Temperature 100·5° F.; pulse 108 per minute, regular, and fairly good volume. Tongue dry, cracked, brown fur; skin and conjunctivæ, jaundice more marked; heart sounds muffled; spleen plus and tender; liver slightly enlarged; hiccough troublesome; no vomiting; no mental symptoms. Seen by the Consulting Physician.

*First blood film:* negative.

6 p.m. Hiccough troublesome; vomited greenish fluid; incontinence of urine and fæces.

*Treatment.*—

10 a.m. Intramuscular quinine 10 grains, champagne 2 ounces.

6 p.m. Intramuscular quinine 20 grains, tinct. iodine 1 minim, repeated, for hiccough.

---

2/10/17—10 a.m. Slept at intervals during night; hiccough persistent; speech clearer, appears to be less drowsy; tongue cleaner; temperature normal; pulse 112 per minute.

*Second blood film :* B.T., rings very numerous.

6 p.m. Hiccough constant; patient vomits at intervals.

*Treatment.*—

10 a.m. Intramuscular quinine 10 grains.

6 p.m. Intramuscular quinine 20 grains, morphia $\frac{1}{4}$ grain, hypodermically; mustard plaster to abdomen.

---

3/10/17—9 a.m. Hiccoughed during sleep; pulse satisfactory.

3 p.m. Hiccough has ceased; pulse poor; pituitrin 1 cubic centimetre.

6 p.m. Respiration shallow and rapid; pulse fast and thready; sudden collapse.

---

*Treatment.*—

9.30 a.m. Intramuscular quinine 10 grains, quinine 15 grains by mouth; ac. hydrocyan. dil. 1 minim; enema, good result.

6 p.m. Intravenous quinine 10 grains in saline 10 ounces, strychnine $\frac{1}{60}$ grain, hypodermically; pulse improved after the intravenous injection, but patient died at 7.30 p.m.

*Post-mortem report.*—Heart muscle soft and atrophied, chambers somewhat dilated, valves normal. Lungs, hypostatic congestion both bases, right upper lobe shows commencing pneumonia, red hepatization. Spleen, three times normal size, very soft indeed, semi-solid and of a dark

chocolate colour. Liver, slightly enlarged, soft, dark green in colour from deposition of pigment. Brain, whole substance peppered with minute petechiæ; other organs, no visible abnormality.

*Report from Base Laboratory on Sections.*—Spleen, completely autolysed, melanin abundant. Brain, no thrombosis present, but capillaries contain numerous malignant tertian parasites (dot type).

*Comments.*—(1) Note the post-mortem report on the heart, brain, spleen and liver.

(2) The marked jaundice, the vomiting of greenish fluid, the persistent hiccough, the drowsiness, and the sudden collapse show the extreme virulence of the infection.

(3) I need not dilate on the treatment except to point out that the patient was admitted before the "large dose method" became the vogue.

Next we have a case with similar symptoms which cleared up on large doses of quinine.

This patient was so ill that for about a week it was very questionable whether there was any chance at all of his recovery. The persistent hiccough and vomiting exhausted him, and he appeared to be gradually going downhill. Many medical officers and nearly all sisters regard persistent hiccough as a sure sign of approaching dissolution. That is what happened in this case; the prognosis was grave in the extreme. The nursing staff, however, reckoned without quinine, and, again, the seemingly impossible happened—the patient recovered.

Case 4. *Bilious malarial fever with extreme jaundice, vomiting, hiccough, and collapse.*—Pte. R., aged 30. Admitted December 4, 1917. In Balkans, one year.

*Previous history.*—Malaria twice, last attack in October, 1917.

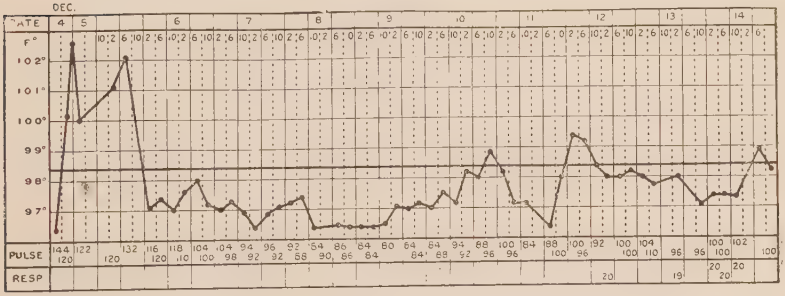
*Onset of present illness.*—Day before admission.

*Symptoms.*—Rigor, fever, vomiting, and a little diarrhœa.

*On admission.*—Temperature 94·6° F., pulse 144. Patient in a collapsed condition; tongue furred; skin jaundiced; heart and lungs normal; spleen enlarged and tender; liver enlarged.

*Treatment.*—Brandy ½ ounce 4-hourly; quinine 15 grains. t.d.s., by mouth.

8 p.m. Intramuscular quinine 20 grains.




Case 4. Private R.

5/12/17—Jaundice more marked; had a poor night, vomited at 2 a.m.

10 a.m. Temperature 102·6° F.; urine contains much bile pigment; vomit contains bile.

5 p.m. Temperature 101·2°, pulse 120; marked jaundice; vomiting.

*Treatment.*—

10 a.m. Intramuscular quinine 20 grains given; brandy 4-hourly continued.

5 p.m. Rectal saline 10 ounces with quinine 20 grains, retained; strichnine $\frac{1}{30}$ grain, digitaline $\frac{1}{100}$ grain 4-hourly.

7 p.m. Intramuscular quinine 20 grains.

10 p.m. Intramuscular quinine 20 grains and champagne.

---

6/12/17—Slept at intervals during night, but vomited a number of times.

10 a.m. Temperature 97·4° F., pulse 120, weak. Patient feels slightly better, but weak; jaundice not quite so marked; has retained a little nourishment; urine contains much albumen, very dark in colour—bile pigment.

9 p.m. Patient improved; pulse stronger, 100 per minute; temperature keeping down.

*Treatment.*—

12 noon. Intramuscular quinine 20 grains.

4 p.m. Rectal saline with quinine 20 grains.

7 p.m. Intramuscular quinine 20 grains.

---

*Bacteriological Report on Fresh Specimen of Urine.*—Spirochætes not found. *Culture:* Growth of enterococcus (probably a contamination).

7/12/17—Vomited once during the night.

10 a.m. Pulse 98 per minute, good; hiccough rather troublesome.

6 p.m. Temperature 97° F., pulse 92.

*Treatment.*—Quinine 15 grains, t.d.s., by mouth.

Noon. Intramuscular quinine 20 grains.

---

8/12/17—Much improved; still jaundiced; temperature sub-normal; pulse 88; urine, only a trace of albumen, no bile. Taking nourishment.

*Treatment.*—

10 a.m. Intramuscular quinine 20 grains; quinine 15 grains, t.d.s., by mouth; strichnine and digitaline discontinued.

9/12/17—Continued improvement; no vomiting; no hiccough.

*Treatment.*—Quinine 15 grains, t.d.s., by mouth.

---

10/12/17—Patient inclined to be a little delirious at times.
*Treatment.*—Quinine 15 grains, t.d.s., by mouth.

---

11/12/17—Patient worse; hiccough troublesome; frequently delirious; tongue coated; more jaundiced; liver not palpable.

*Treatment.*—

10 a.m. Intravenous quinine, 20 grains, in saline 8 ounces.

6 p.m. Intravenous quinine, 20 grains, in saline 8 ounces.

10 p.m. Intramuscular quinine, 20 grains.

---

12/12/17—Temperature 99·2° F., pulse 100.

*Treatment.*—

10 a.m. Intravenous quinine, 20 grains, in saline 8 ounces.

6 p.m. Intramuscular quinine, 20 grains.

---

13/12/17—About the same.

6 p.m. Patient seems rather better; tongue much more moist.

*Treatment.*—

10 a.m. Intravenous quinine, 20 grains, in saline, 8 ounces.

6.30 p.m. Intramuscular quinine 20 grains given.

---

14/12/17—Improvement.

6 p.m. Patient much brighter, but hiccough still troublesome; hiccough relieved somewhat when he lies on his "stomach"; tongue much cleaner.

*Treatment.*—

10 a.m. Intravenous quinine 20 grains in saline 8 ounces.
6 p.m. Quinine 15 grains by mouth.
10 p.m. Intramuscular quinine 20 grains.

---

15/12/17—Slight improvement; occasional vomiting; hiccough has not been so troublesome to-day.

*Treatment.*—

11 a.m. Intravenous quinine 20 grains.
5 p.m. Intramuscular quinine 20 grains.
8.30 p.m. Intramuscular quinine 20 grains.

---

16/12/17—Occasional hiccough and vomiting and not quite so jaundiced; cough rather troublesome, thick muco-purulent sputum; scattered râles, no dulness.

*Treatment.*—

11 a.m. Intravenous quinine 40 grains in saline 8 ounces.
9 p.m. Intramuscular quinine 20 grains.

---

17/12/17—Improving; no hiccough; no vomiting.

*Treatment.*—

10 a.m. Intramuscular quinine 20 grains.
6 p.m. Intramuscular quinine 20 grains.

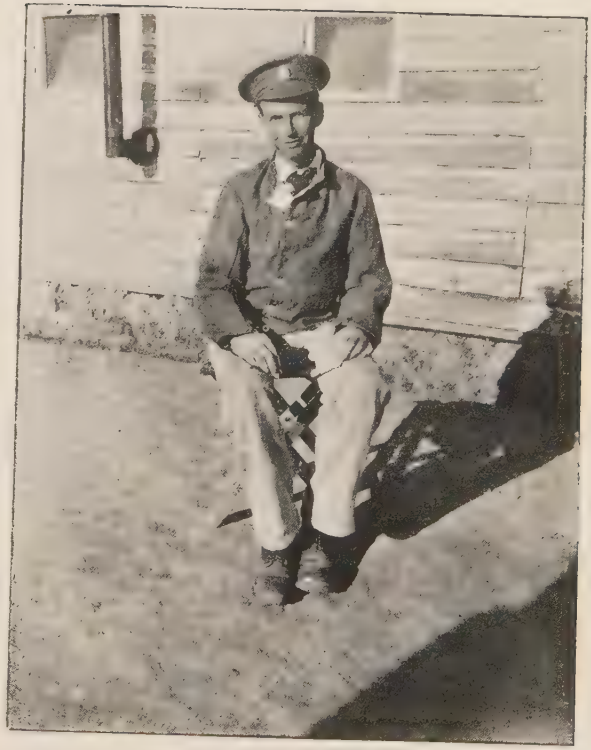
---

18/12/17—Brighter.

*Treatment.*—

9 a.m. Quinine bihyd. 15 grains by mouth, not vomited.
3 p.m. Intramuscular quinine 20 grains.
6 p.m. Intramuscular quinine 20 grains.
10 p.m. Quinine bihyd. 15 grains by mouth, not vomited.

CASE 4.—Private R. Bilious remittent fever. "The prognosis was rave in the extreme."



CASE 4.—Private R. After recovery from bilious remittent fever.

19/12/17—Improving slowly.

*Treatment.*—Quinine 15 grains by mouth, twice. Intravenous quinine 30 grains in 10 ounces of normal saline.

---

20/12/17—Better in every way; no vomiting or hiccough since receiving the intravenous of quinine 40 grains on the 16th inst.

*Treatment.*—Quinine 15 grains, t.d.s., daily.

---

28/12/17—Steady improvement; jaundice very slight.

---

6/2/18—Has had quinine 15 grains, t.d.s., by mouth for the last six weeks, and has quite recovered; no jaundice and no anæmia.

*Comments.*—Patient received an average of 67 grains quinine a day for the first five days after admission and improved slowly.

On December 12, 1917, he had stopped hiccoughing and vomiting, and was put on to quinine 45 grains a day by mouth. The next day he became a little delirious; on December 11 he started to hiccough again, was more jaundiced and frequently delirious, commencing cerebral. He then got two intravenous injections and one intramuscular (quinine 60 grains in the day).

On the 16th as he was not improving to my liking I gave him an intravenous of quinine, 40 grains. This amount is the largest that should be given as a single dose by any route whatsoever, and should only be used in cases of emergency. After this he improved fairly rapidly, stopped hiccoughing and vomiting, and his natural colour returned.

Although the ultimate result in this case was satisfactory, we should have pushed the quinine more vigorously and used the intravenous method more freely in the early stages.

It will be seen that when the quinine was reduced to 45 grains a day by the mouth on December 9 he had a set back, and until we had controlled the condition by larger doses, and in a more direct manner, he showed little sign of real improvement.

Notwithstanding the fact that the treatment in this case leaves much to be desired, it is a masterpiece compared with that of Case 3, Private P.

*Comparison between the Cases of*

| Private P. (Case 3) | and | Private R. (Case 4). |
|---|---|---|
| Admitted September 29, 1917. | | Admitted December 4, 1917. |
| Jaundice and vomiting. | | Jaundice and vomiting. |
| Hiccough for three days. | | Hiccough for a week. |
| Drowsiness and other symptoms of cerebral malaria ending in collapse and death. | | Delirium showing commencing cerebral malaria treated by the correct method to stop the progress of the attack and save the patient's life. |
| *Treatment.*—An average of 40 grains of quinine a day in four days :— Oral. 60 grains Intramusc. 90 grains Intraven. 10 grains | | *Treatment.*—An average of 60 grains a day for sixteen days :— Oral. 300 grains Intramusc. 380 grains Intraven. 190 grains Per rectum—40 grains |
| Only one intravenous—on the last day (10 grains). | | An intravenous of 40 grains of quinine was given on the thirteenth day of illness. |

SCALE OF DOSES RECOMMENDED IN BILIOUS REMITTENT FEVER.

(Quinine bihyd. 20 grains per dose for each injection.)

*First week* of disease : Quinine 60 to 80 grains a day. On first and second days, two intravenous quinines and

one or two intramusculars each day. Third to seventh day inclusive, one intravenous quinine, one intramuscular quinine and one or two rectal quinine salines (20 grains in 8 ounces of normal saline) daily.

*Second week* of disease : Quinine 40 to 60 grains a day by intramuscular or rectal routes.

*Third week and onwards :* Quinine 15 grains, t.d.s., by mouth.

The treatment will be influenced to some extent by the progress made.

## CHAPTER VII.

## THE TREATMENT OF CHRONIC MALARIA.

AFTER the acute stage has passed treatment by quinine should be continued over a long period depending upon the virulence of the infection.

Benign tertian and quartan malaria yield more readily than malignant tertian.

The crescents of the latter variety are extremely resistant to treatment of any kind, and quinine appears to have little or no effect on them. To overcome this difficulty it is necessary to saturate the system with quinine in order to have a sufficient quantity of the drug ready in the circulation to kill the young trophozoites, young schizonts and merozoites whenever sporulation takes place; by this means the formation of crescents and toxins is prevented.

### QUININE IN CHRONIC MALARIA.

*Quinine Statistics of seventy-seven Hospital Ship Cases.*—These men were detained in this hospital for two or three months awaiting embarkation, and were ultimately taken off the hospital ship list because of the extraordinary improvement they had made on quinine during this period.

Of these cases, there are two series A and B :—

(*A*) Fifty-one cases (treated in one set of marquees).

(*B*) Twenty-six cases (treated in another set of marquees).

*Series A.*—Quinine statistics in regard to this series are

unfortunately of little use, because the quinine issue for twenty-seven days was irregular, and it is impossible to say how much quinine these men really had. This is due to the fact that the medical officer who was temporarily attached here and was given the supervision of these patients, either misunderstood the order to keep them on quinine, 30 grains a day, or had views of his own on the subject. The result is that during the time he had charge of the cases, there were fourteen relapses. The average period between the time he started his treatment—which consisted of quinine 0 to 10 grains a day—and the relapse, was fifteen days.

My attention was drawn to the fact that something was wrong with the treatment in these tents by the number of relapses that were occurring.

*Series B.*—One of my most reliable medical officers had charge of these patients, and the figures given below are absolutely accurate.

| Name | Blood film | Number of grains of quinine | Number of days treated |
|---|---|---|---|
| Pte. W. ... | Malignant tertian ... | 1680 | 42 |
| ,, G. ... | ,, ,, ... | 2640 | 71 |
| ,, M. ... | Negative ... ... | 2520 | 74 |
| ,, S. ... | No slide ... ... | 1940 | 50 |
| Sgt. G. ... | Malignant tertian ... | 1880 | 56 |
| Pte. M. ... | No slide ... ... | 2940 | 75 |
| ,, P. ... | Mononuclear increase | 2400 | 74 |
| ,, M. ... | Negative ... ... | 2730 | 81 |
| ,, M. ... | Malignant tertian ... | 3400 | 91 |
| ,, T. ... | Mononuclear increase | 2450 | 80 |
| Cpl. D. ... | Negative ... ... | 2480 | 72 |
| Pte. K. ... | ,, ... ... | 2520 | 76 |
| ,, H. ... | No slide ... ... | 2220 | 57 |
| ,, R. ... | Type undetermined ... | 3560 | 91 |
| ,, W. ... | Malignant tertian ... | 2170 | 68 |

| Name | Blood film | Number of grains of quinine | Number of days treated |
|---|---|---|---|
| Pte. D. ... | Malignant tertian ... | 1330 | 31 |
| „ H. ... | Negative ... ... | 1930 | 54 |
| „ G. ... | Benign tertian ... ... | 2530 | 75 |
| „ Y. ... | Malignant tertian ... | 2880 | 82 |
| Cpl. B. ... | Type undetermined ... | 3000 | 91 |
| Pte. B. ... | Mononuclear increase | 2340 | 64 |
| „ H. ... | „ „ | 3310 | 94 |
| „ E. ... | „ „ | 2760 | 78 |
| „ B. ... | „ „ | 1440 | 68 |
| „ C. ... | Negative ... ... | 2630 | 77 |
| „ M. ... | Mononuclear increase | 2700 | 80 |

Average dose of quinine a day = 35 grains.

Average number of days quinine was given = seventy-one days.

*Comments.*—Two relapses only in this series :—

(1) Pte. McC., blood film negative, relapsed on December 13, 1917 after taking 2,500 grains in seventy-six days, average 33 grains a day.

When he left this hospital on December 18, 1917, his spleen was still enlarged and tender.

I received a letter from him on January 22, 1918, from Malta, saying that he had had no quinine since leaving Salonika, relapsed two days after reaching Malta, and received three intravenous injections of quinine.

I am of opinion that a daily ration of quinine (30 grains) continued for a couple of months after leaving this hospital might have prevented a relapse sufficiently severe to necessitate intravenous injections of quinine.

(2) Pte. R., blood film "type undetermined," very slight relapse on December 12, 1917. This was a very cold day. His temperature rose to 101° F., but he had no rigor.

It is questionable whether this was a genuine relapse. It occurred after the patient had taken 3,350 grains in eighty-seven days, average 38 grains a day.

Blood films were taken in all these cases on the day before they were discharged (December 17, 1917). Two were positive, but neither of these had relapsed:—

(1) Sgt. G., blood film, malignant tertian,—young trophozoites. This was after taking 1,880 grains in fifty-six days. Average, 34 grains daily.

(2) Pte. M., blood film, malignant tertain,—gametes. This was after taking 3,400 grains in ninety-one days, average 38 grains a day.

It is interesting to find that, although both these men had parasites in the peripheral circulation, the quinine they had taken prevented them from relapsing.

*Note.*—(1) That the successful treatment of malaria, either in the acute or chronic stage, depends upon the amount of quinine given and the method used to assure its absorption.

(2) That the malignant tertian type, being less amenable to treatment, requires larger doses and a longer course of quinine treatment than other varieties.

(3) That the state of the spleen (seen post-mortem) makes it very evident that this condition will not clear up without vigorous and prolonged quinine treatment.

(4) That if malarial patients were treated vigorously with quinine in the early stages of the disease, no lives would be lost, and the percentage of chronic malaria with anæmia and enlarged spleens requiring prolonged courses of treatment with quinine, arsenic and galyl would be reduced to within reasonable limits.

Since writing the above six weeks ago, I have received letters from eleven of the seventy-seven hospital ship

cases saying that they have had little or no quinine since leaving here, and have all relapsed.

One patient was re-admitted to this hospital on February 25, 1918, in a condition which made it quite evident from the first that he had no chance of recovery. This was Corporal M. the record of whose case will be found under "blackwater fever."

This man was boarded in November last, but improved so much on quinine treatment that we removed him from the hospital ship list, and in December he was sent back to his unit to await an opportunity of returning to England by ordinary transport. While in this hospital, although he was a proved malignant tertian case with a very enlarged spleen, he had no relapse, due to the fact that he received 1,755 grains of quinine in fifty-one days —average 34 grains daily.

During the forty-five days after discharge he received about 685 grains—average 15 grains daily. He relapsed constantly, and when he was re-admitted here was found to be in an extremely toxic condition and dying from blackwater fever. The quinine he had had was inadequate and quite unable to destroy the parasite and prevent the formation of malaria toxins in his blood.

Deaths will occur until people realize the necessity for using quinine in malaria. Giving 15 grains a day in chronic malignant tertian malaria is not using the drug, it is merely playing with it.

The post-mortem report on the organs of this patient is highly instructive and worthy of careful study (*vide* pp. 218-19).

### *The Duration of Quinine Treatment.*

The duration of treatment depends on a variety of conditions of which the most important are :—

(1) The type of parasite—the benign tertian being more amenable to treatment than the malignant tertian.

(2) The degree of virulence of any one type of parasite, e.g., the malignant tertian parasites may be more numerous and generate more toxins in one set of circumstances than in another.

(3) The power of resistance to the parasite and its toxins by the individual; that is, the amount of antitoxin formed varies in different persons.

(4) The question of efficient quinine treatment in the early stages. The more chronic the condition is allowed to become the less likely it is to clear up quickly.

The method to adopt is to keep the patient on 45 grains a day for a month. If he relapses during this time, it is evident he is not receiving sufficient quinine to kill the parasites in the blood; therefore, the amount of quinine is increased to 60 grains a day for a week. As the patient improves, the quinine is gradually reduced to 30 grains a day, and this dosage is kept up until the spleen has become normal, all tenderness has disappeared, and there has been no relapse for at least three months.

If after this the patient relapses, the condition must be looked upon as an extremely malignant one, and a further course of treatment for three months started. If, in addition, a course or two of mist. arsen. tonic is given, even the worst types of case do extraordinarily well.

The rule to remember is that a relapse means that the patient requires more quinine to overcome the parasite in the circulation.

*Arguments advanced Against the Use of Large Doses of Quinine.*

(1) It is said that patients complain of giddiness and inability to work when taking 30 to 45 grains a day.

I have found that patients begin to tolerate quinine after taking it for a while, the deafness and giddiness passes off, and the malaria being kept under control, the man's general condition improves.

*Note.*—The deafness may be treated with bromides.

(2) Patients complain of the taste and say it makes them feel nauseous. I am quite convinced that the taste of the drug has been, and still is, one of the greatest factors against its free use in malaria. If quinine were pleasant to take, scientists would have realized years ago how extraordinarily safe and efficacious large doses of quinine over a prolonged period are. I am afraid medical men pander to the idiosyncrasy of the individual and are too apt to believe a patient who says the drug makes him feel "sick" and does him no good, simply because he loathes the taste of it.

(3) Some authorities contend that to give certain doses of quinine as a routine in all cases, whatever the type of the malaria may be, is not scientific and therefore inadmissible. Ever since the time that cinchona bark was introduced into Europe by the Countess of Chinchon (17th century) men have argued, and theories have been advanced, on the subject of the scientific administration of quinine. The arguments still continue, while the patients die.

Clinically, I find that if the disease is treated in the manner and with the doses I suggest, the patients improve in both the acute and chronic stages, and ultimately recover; while patients treated with quinine in various other ways, based upon theory, come back to us wrecked in health, dying or dead, and the post-mortem findings show that they have succumbed to some form of malarial toxæmia.

(4) Medical officers assert that it is difficult to treat

patients with large doses of quinine over a period of many months. Yet, before the introduction of salvarsan, patients took large doses of potassium iodide daily not only for months, but for years, in order to cure themselves of syphilis. Potassium iodide is not so unpleasant to take which is probably the reason why it was so freely used.

(5) Another argument against quinine is that it tends to make the patient anæmic. That is, of course a fallacy.

I append the results of the blood counts and hæmoglobin percentage in a number of malaria cases after taking 30 to 45 grains a day for from two to three months. These men did not receive arsenic or any other blood tonic during the time.

| Name | Hb. | R.B.C. | Colour index |
|---|---|---|---|
| Pte. F. ... | 76 per cent. | 3,260,000 per c.mm. | 1·1 |
| ,, B. ... | 82 ,, | 4,430,000 ,, | 0·93 |
| ,, G. ... | 74 ,, | 3,460,000 ,, | 1·1 |
| ,, J. ... | 92 ,, | 4,500,000 ,, | 1·0 |
| ,, S. ... | 92 ,, | 4,880,000 ,, | 0·94 |
| ,, F. ... | 73 ,, | 4,200,000 ,, | 0·9 |
| ,, F. ... | 90 ,, | 4,610,000 ,, | 1·0 |
| ,, R. ... | 90 ,, | 5,200,000 ,, | 0·9 |
| ,, W. ... | 80 ,, | 4,860,000 ,, | 0·82 |
| ,, K. ... | 90 ,, | 4,100,000 ,, | 1·1 |
| ,, L. ... | 86 ,, | 3,744,000 ,, | 1·16 |
| ,, K. ... | 80 ,, | 3,320,000 ,, | 1·2 |

It must be borne in mind that these were all cases of chronic malaria who had had many relapses and been subjected to considerable blood destruction by the malaria parasites.

The blood results, therefore, after treatment with quinine alone, are very satisfactory.

After careful consideration of the facts and results I have put forward, I think that even the most biased critic will admit that, failing some totally new discovery in regard to the treatment of malaria, the method to use is the one that shows the best results clinically. Large doses of quinine over a prolonged period destroy the parasite and prevent chronic toxæmia with its accompanying damage to the organs of the body and liability to sudden death from cardiac failure, blackwater fever, &c.

This line of treatment, therefore, should be definitely laid down in the Army, while civilian practitioners should consider the advisability of a drastic change in views on quinine dosage and the evils which are supposed to result from giving large amounts of the drug.

Man should not be allowed to die from neglected malaria when it is easy enough to prevent death by rational treatment with quinine.

### *The Treatment of Women suffering from Malaria.*

Quinine affects the uterus and increases the menstrual flow in some women. It is necessary, therefore, to modify the dosage somewhat in these cases. This does not apply to cerebral and other complications of malaria in which the maximum doses are required in order to save the patient's life.

*Change of Climate.*—Persons suffering from chronic malaria, especially those who have had cerebral, blackwater or other pernicious forms of malarial fever, should not be allowed to remain in malarial regions, because of the danger of reinfection. A change to a non-tropical country, where there are no anopheline mosquitoes, improves the general health of the patient and is of great value in treatment.

AT AN ADVANCED DRESSING STATION.

Travois with patient on stretcher, and mule with a pair of cacolets (folding chairs hooked on to a pack saddle) going out to fetch a couple of sitting cases.

CROSSING A ROUGH MOUNTAIN PASS.

Cacolet mule carrying two seriously ill cases. Pass too rough even for a travois.

Travois conveying a Lying Case over Bad Ground to an Advanced Dressing Station.

The two men with ropes in the rear are there for the purpose of keeping the travois from slipping off the path.

Wheeled Stretcher, Mark I,

Fitted with hood (Woolwich pattern) and mosquito curtains, in a Turkish village just behind the firing line. This conveyance is used when the roads are fairly good.

### Chronic Malaria on the Struma Front.

It is necessary to explain that a few months after writing the above, on account of the attitude of the authorities in regard to a case of blackwater fever which occurred in my division, I sent in my resignation, and for the last two months have been attached to a field ambulance. For a part of this time I acted as regimental medical officer to a battalion in the line and have been able to obtain a considerable amount of information in regard to malaria in the battalions on this Front.

I find that the treatment of malaria during the first five months of this year (1918) has been left to the discretion of the medical officer of the unit. Many of the medical officers at the Front have had very little experience of the disease, due to the fact that they only treat ordinary relapses. All serious cases have to be evacuated to the base hospitals labelled "pyrexia of unknown origin," the medical officer not being allowed to diagnose the condition as malaria.

The one I relieved gave sufficient quinine to tide over the relapse and then sent the man back to duty without further treatment.

The following summary of a report written by me, on May 15, 1918, at the request of the Officer Commanding the 3rd Battalion may be of interest :—

"Reference my conversation with you about malaria in your unit I have to report that about 90 per cent. of the men have had malaria. Of this percentage 583 reported sick between January 1 and May 15, 1918. Since reporting, 460 of these have had one, two or more relapses; all of them have enlarged, palpable, or tender spleens and most have some degree of anæmia and tachicardia. The figures I have given you above show that notwithstanding over two years' experience in

Macedonia, the treatment of malaria has completely broken down.

"Last year an effort at treatment was made in the right direction. An average of 20 grains of quinine a day for three months was given as a routine to a large number of the troops in the division, this failed to prevent relapses simply because it did not go far enough.

"I have the following advice to submit based on ten years' experience in Africa and eighteen months careful study of the subject in Macedonia.

"To treat malaria successfully there are four essentials :—

"(1) That the patient receives his quinine regularly.

"(2) That he absorbs it.

"(3) That he takes sufficient quinine a day to destroy the parasite in the blood and prevent the formation of the toxins.

"(4) That he takes it over a long enough period to cure him, especially in the very chronic cases.

"Although quinine is at first unpleasant to take men soon tolerate it, and it is essential to use it freely to prevent the malarial toxæmia which damages the patient's internal organs, makes him useless as a soldier and may cause his death.

"*Method of Treatment.*—A quinine roll should be kept and every man who has had a relapse this year should be placed on it.

"The men should be paraded and given quinine in solution morning, noon and evening, or morning, late afternoon and the last thing at night, as convenient.

"*Period of Treatment.*—Five months, through the summer and autumn.

"*Dosage.*—Quinine bi-hydrochloride, or sulphate 10 grains three times a day. Men who relapse on this

should have their quinine increased to 15 grains three times a day for a fortnight at least, before returning to 30 grains a day. A few will relapse on 45 grains a day; in the case of these extremely chronic malarial patients the quinine should be increased to 60 grains a day for a week.

"I have had most extraordinarily good results from prolonged treatment with these doses. It will be found that men can do more and better work than they could possibly do if allowed to relapse constantly.

"The quinine, especially if combined with iron and arsenic, improves their general health, clears up the anæmia by preventing blood destruction, and gradually cures the malaria.

"The method of simply treating the relapse without endeavouring to cure the patient besides being obsolete is extremely dangerous; the more chronic a case of malaria is the more liable it is to become cerebral, or to develop blackwater fever and other very serious complications."

I also wrote to the A.D.M.S. Division asking him to bring the matter before the D.D.M.S. Corps.

The following is a copy of the letter:—

"For your information I enclose a report on malaria which I wrote for the officer commanding 3rd battalion. In support of my arguments for continued larger doses of quinine I have to point out that when a malaria patient at a base hospital is very seriously ill he is given large doses of quinine over a long period. I have given a patient suffering from post-malarial tremors and inability to use either his arms or legs, 100 grains of quinine a day for five days, followed by 45 grains a day for forty-four days and 30 grains a day for a further twenty-eight days. Of these amounts he received 3,025 grains by the mouth, 215 intramuscularly and 80 grains intravenously.

"Total amount of quinine taken was 3,320 grains in seventy-seven days, a daily average of 43 grains.

"This patient made a complete recovery and was able to walk about and use his arms freely before being sent to England. The case is only one of hundreds which I treated with these large doses of quinine when I was officer commanding the medical division of a General Hospital last year. For the four months prior to my being transferred from this hospital every malarial patient admitted received at least 45 grains a day during the whole of his stay, and my results could not be improved upon. Last summer and autumn the base hospitals were full up, chiefly with malaria. Many patients died, and medical officers and staffs of hospitals and other medical units were called upon to do more work than legitimately could be expected from them. I am of opinion that a good deal of this could be prevented this year by using the doses I advise in my letter to the Officer Commanding 3rd Battalion."

---

A point I omitted to mention in this letter is that the treatment would also tend to prevent men becoming reinfected. The best time to take quinine for the latter purpose is while or just after the mosquitoes are biting, early in the morning, in the evening, and the last thing at night. This gives the drug a chance to act before being excreted. I do not, however, suggest the use of prophylactic quinine in the ordinary way. A man who has not had an attack should take every precaution to prevent being infected.

---

I regret very much that the authorities have not deemed it expedient to test the methods of treatment embodied in the above letters. Hundreds of thousands of men have contracted malaria since joining the Army, and as

the majority of these will return to civilian life when the war is over, they should be discharged as fit as possible to enable them to hold their own in the struggle for existence which is coming. The Army system is an ideal one from the standpoint of facilities for treating disease; the men are under constant medical supervision, and given a free hand, there is no difficulty in carrying out any treatment which may be considered advisable. After discharge, however, the troops will be scattered far and wide, and although, by compulsory notification and careful organization, it will be possible to do a great deal towards eradicating malaria, still the main effort should be made before the men leave the Army.

Apart from the effect on the individuals the danger to the health of their relatives, friends, and the community in general should be considered. Every man who has the malaria parasite in his blood may become a source of infection in any part where there are anopheles moquitoes.

A serious epidemic of malaria in the British Isles after the war is quite within the bounds of possibility, unless steps are taken at once to deal with the problem.

## CHAPTER VIII.

### MALARIAL ANÆMIA.

Malarial anæmia is the result of chronic malaria with repeated relapses which have been inadequately treated with quinine.

The indications are: General weakness. Marked anæmia. Skin and conjunctivæ, icteric tinge; this may be absent. Spleen enlarged and generally tender. Liver, may or may not be enlarged and tender. Heart, functional bruits sometimes heard. Generally a faint mitral systolic—not propagated, or a hæmic murmur in the pulmonary area. Hæmoglobin, varying from 20 per cent. to 60 per cent. Red blood corpuscles numbering from 1½ to 3 millions.

Treatment.—Quinine 45 to 60 grains a day for the malaria; and galyl, or arsenic by mouth in graduated doses, for the anæmia.

*Galyl* is a compound of arsenic similar to neosalvarsan but more than double the strength. It is sold in boxes which hold an outfit consisting of a cylindrical phial containing a yellowish-green powder—the galyl—(fig. 1), an ampoule of sterile carbonated serum (fig. 2), a file (fig. 3), and a small rubber disc (fig. 4).

*Note.*—Should the powder be dark in colour, it shows that the galyl has undergone decomposition and should be rejected.

*Galyl Solution.*—Twenty centigrammes (·2 gramme) of galyl in 4 ounces of sterile distilled water is the standard

solution for use in malarial anæmia in which the heart muscle is generally weak and atonic. This dose may be repeated two or three times as required, at intervals of five or six days.

*Preparation of the Solution.*—(1) Make a file mark on the neck of the bottle and break off the end.

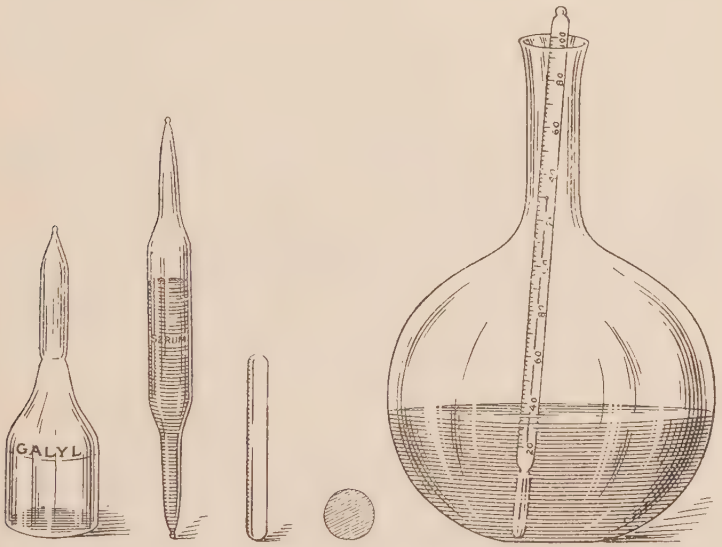



Fig. 1. Fig. 2. Fig. 3. Fig. 4. Fig. 5, Galyl Solution ready for use.

(2) File and remove the ends of the ampoule and allow the serum to run into the phial.

(3) Place the rubber disc over the mouth of the bottle, hold it firmly in position between the finger and thumb and shake well until the galyl has dissolved in the serum. The resulting solution should be yellow or brownish-yellow in colour.

(4) Pour this into a large glass flask containing 4 ounces of sterile water—distilled if possible—and shake until the mixture is a clear greenish-yellow colour (fig. 5).

*Technique for Administration.*—The apparatus and the method of giving intravenous galyl are exactly the same as those for intravenous quinine (see p. 43).

*Points to be Observed.*—First, run 2 ounces of sterile normal saline solution into the vein to make certain that the point of the needle is in its lumen ; galyl in the subcutaneous tissue causes unnecessary pain and swelling.

Next, the 4 ounces of galyl solution are passed into the circulation.

Finally, a couple of ounces of sterile water are injected in order to wash the remains of the galyl through the tube.

The operation is completed by sealing up with collodion in the usual way.

*Arsenic by Mouth.*—A little iron and nux vomica combined with the arsenic may be of advantage.

The following is the prescription we use in this hospital :—

*Mist. Arsen. Tonic.*

| | | | |
|---|---|---|---|
| ℞ Liq. arsenici hyd. | ... | ... | 1 minim |
| Ferri et ammon. cit. | ... | ... | 1 grain |
| Tinct. nucis vom. | ... | ... | ½ minim |
| Aq. chlorof. | ... | ad | 1 drachm |

Misce et fiat mistura.

Sig. : Three drachms as the initial dose, t.d.s., p.c., increased by 1 drachm per dose every second day to a maximum of 8 drachms t.d.s., unless contraindicated.

When the patient has received the maximum dosage for a couple of days, the medicine is stopped for four days. After this, he is put on to a second, and if necessary, a third course, commencing each time with the minimum dose (3 drachms t.d.s.). This precludes the possibility of peripheral neuritis and other manifestations of arsenical poisoning.

*Note.*—A course of treatment by mist. arsenic tonic takes sixteen days to complete, i.e., twelve days during which the drugs are administered, and then an interval of four days.

*The relative value of Galyl and Arsenic by the Mouth.*—A knowledge of the effects of treatment by galyl compared with arsenic by the mouth in malarial anæmia is of great importance, on account of :—

(1) The expense.

(2) The fact that the latter is so much more easily administered.

In order to arrive at a decision in the matter, I collected a number of cases in one ward, treated some with galyl and others with mist. arsenic tonic, and compared the results.

Although it is not possible to go into the details of all these, I propose to submit notes showing the blood changes in a series of twenty cases. Of these, ten were treated by the one method, and the rest by the other. They all received quinine 15 grains t.d.s., as well.

With a view to eliminating the personal factor, all blood counts and hæmoglobin estimations were done by the same bacteriologist.

It should be noted that in order to assure accurate results the hæmoglobinometer was tested on several apparently normal persons who had never had malaria, and in each case their hæmoglobin was found to be 100 per cent.

*Treatment by Galyl.*—No. 1—Rifleman F. (galyl, two doses). Admitted on November 24, 1917, suffering from malaria. Malaria six times.

*Blood film :* Benign tertian (numerous rings and trophozoites).

| | | |
|---|---|---|
| 30/11/17. | Hæmoglobin ... ... | 65 per cent. |
| | Red blood corpuscles... | 3,400,000 per c.mm. |
| | Colour index ... ... | 0·95 |
| 5/12/17. | Galyl 0·2 gramme given intravenously. | |
| 10/12/17. | Hæmoglobin ... ... | 80 per cent. |
| 13/12/17. | Galyl 0·2 gramme given intravenously. | |
| 19/12/17. | Hæmoglobin ... ... | 90 per cent. |
| 20/12/17. | Red blood corpuscles... | 4,000,000 per c.mm. |
| | Colour index ... ... | 0·89. |

*Final Result.*

Hæmoglobin improvement = 25 per cent.

Red blood corpuscle improvement = 600,000 per c.mm.

---

No. 2—Corporal B. (galyl, two doses). Admitted on November 21, 1917, with a rigor. Malaria constantly for four months.

*Blood film:* Malignant tertian gametocytes.

| | | |
|---|---|---|
| 1/12/17. | Hæmoglobin ... ... | 56 per cent. |
| | Red blood corpuscles... | 3,576,000 per c.mm. |
| | Colour index ... ... | 0·78 |
| 6/12/17. | Galyl 0·175 gramme intravenously. | |
| 10/12/17. | Hæmoglobin ... ... | 64 per cent. |
| 18/12/17. | Galyl 0·2 gramme intravenously. | |
| 27/12/17. | Hæmoglobin ... ... | 66 per cent. |
| 3/1/18. | Hæmoglobin ... ... | 70 per cent. |
| | Red blood corpuscles... | 3,768,000 per c.mm. |
| | Colour index ... ... | 0·93 |
| 10/1/18. | Hæmoglobin ... ... | 90 per cent. |
| 13/1/18. | Hæmoglobin ... ... | 90 „ |
| | Red blood corpuscles... | 4,680,000 per c.mm. |
| | Colour index ... ... | 1·04 |

*Final Result.*

Hæmoglobin improvement = 34 per cent.

Red blood corpuscle improvement = 1,104,000 per c.mm.

No. 3—Driver W. (galyl, two doses). Admitted on December 1, 1917. Malaria July, 1916, August and November, 1917. Very anæmic. Spleen, much enlarged (2 inches below costal margin).

*Blood film* shows polychromatophilia.

| | | |
|---|---|---|
| 2/12/17. | Hæmoglobin ... ... | 42 per cent. |
| | Red blood corpuscles... | 1,600,000 |
| | Colour index ... ... | 1·3 |
| 7/12/17. | Galyl 0·175 gramme intravenously. | |
| 10/12/17. | Hæmoglobin ... .. | 48 per cent. |
| 14/12/17. | Galyl 0·2 gramme intravenously. | |
| 19/12/17. | Hæmoglobin ... ... | 82 per cent. |

After this date, patient was attending the dentist for extraction of septic stumps.

| | | |
|---|---|---|
| 10/1/18. | Hæmoglobin ... ... | 90 per cent. |
| 22/1/18. | Hæmoglobin ... ... | 85 ,, |
| 27/1/18. | Hæmoglobin ... ... | 75 ,, |
| | Red blood corpuscles... | 3,450,000 per c.mm. |
| | Colour index ... ... | 1·1 |

*Final Result.*

Hæmoglobin improvement = 33 per cent.

Red blood corpuscle improvement = 1,850,000 per c.mm.

*Comments.*—I cannot account for the diminution in the hæmoglobin after January 10, 1918. It was probably due to the condition of his teeth.

---

No. 4—Driver S. (galyl, two doses). Admitted on November 1, 1917. Anæmic after malaria.

*Blood film :* Rings. Type undetermined.

| | | |
|---|---|---|
| 1/12/17. | Hæmoglobin ... ... | 62 per cent. |
| | Red blood corpuscles... | 3,680,000 per c.mm. |
| | Colour index ... ... | 0·84 |

| | | |
|---|---|---|
| 7/12/17. | Galyl 0·2 gramme intravenously. | |
| 10/12/17. | Hæmoglobin ... ... | 52 per cent. |
| 13/12/17. | Hæmoglobin ... ... | 62 „ |
| 18/12/17. | Galyl 0·2 gramme intravenously. | |
| 20/12/17. | Hæmoglobin ... ... | 70 per cent. |
| 27/12/17. | Hæmoglobin ... ... | 72 „ |
| 3/1/18. | Red blood corpuscles... | 3,500,000 per c.mm. |
| 10/1/18. | Hæmoglobin ... ... | 96 per cent. |
| | Red blood corpuscles... | 4,400,000 per c.mm. |
| | Colour index ... ... | 1·09 |

*Final Result.*

Hæmoglobin improvement = 34 per cent.

Red blood corpuscle improvement = 720,000 per c.mm.

*Note.*—The fall in the hæmoglobin percentage on December 10, 1917, may possibly have been due to an error in estimation, as the patient had not had a relapse to account for it.

---

No. 5—Private H. Treated with galyl and also with mist. arsen. tonic. From October 24, 1917, to December 2, 1917, patient had had malarial relapses lasting for from two to six days, with intervals of a few days during which the temperature was normal. This was probably a double infection, and patient became progressively anæmic. Admitted—General Hospital on November 28, 1917. Given quinine 20 grains t.d.s.

| | | |
|---|---|---|
| 4/12/17. | Quinine reduced to 15 grains t.d.s. | |
| | *Blood film :* Rings ; type undetermined. | |
| 6/12/17. | Hæmoglobin ... ... | 62 per cent. |
| | Red blood corpuscles... | 3,968,000 per c.mm. |
| | Colour index ... ... | 0·78 |
| 8/12/17. | Galyl 0·2 gramme given intravenously. | |
| 13/12/17. | Hæmoglobin ... ... | 70 per cent. |

| | | |
|---|---|---|
| 3/1/18. | Hæmoglobin ... ... | 70 per cent. |
| | Red blood corpuscles... | 3,112,000 per c.mm. |
| | Colour index ... ... | 1·1 |
| 8/1/18. | Slight rigor and rise of temperature. | |
| 10/1/18. | Hæmoglobin ... ... | 86 per cent. |
| 22/1/18. | Hæmoglobin ... ... | 75 „ |
| 25/1/18. | Mist. arsen. tonic t.d.s. (graduated doses). | |
| 7/2/18. | Hæmoglobin ... ... | 90 per cent. |
| | Red blood corpuscles... | 4,340,000 per c.mm. |
| | Colour index ... ... | 1·04 |
| 18/2/18. | Hæmoglobin ... ... | 100 per cent. |
| | Red blood corpuscles... | 5,120,000 per c.mm. |
| | Colour index ... ... | 1·0 |

*Final Result.*

Hæmoglobin improvement = 38 per cent.

Red blood corpuscle improvement = 1,152,000 per c.mm.

*Note.*—(1) The striking change for the better in the blood picture notwithstanding the relapse.

(2) The improvement in a month on one injection of galyl, and during a similar period on one course of mist. arsen. tonic, tends to show that the latter is quite as efficacious as galyl.

---

No. 6—Private M. History of irregular remittent temperature for last two months in another hospital. Had quinine 30 grains daily all this time. Blood film : Malignant tertian positive. Admitted on November 18, 1917. Very anæmic. Spleen, much enlarged. *Blood film :* Malignant tertian gametocytes.

| | | |
|---|---|---|
| 1/12/17. | Hæmoglobin ... ... | 42 per cent. |
| | Red blood corpuscles... | 3,500,000 per c.mm. |
| | Colour index ... ... | 0·6 |
| 8/12/17. | Galyl 0·2 gramme intravenously. | |

| | | |
|---|---|---|
| 13/12/17. | Hæmoglobin ... ... | 64 per cent. |
| 17/12/17. | Galyl 0·2 gramme intravenously. | |
| 19/12/17. | Hæmoglobin ... ... | 70 per cent. |
| 27/12/17. | Hæmoglobin ... ... | 70 „ |
| 3/1/18. | Red blood corpuscles... | 3,350,000 per c.mm. |
| 8/1/18. | Slight relapse. Intramuscular injection of quinine given in addition to the 45 grains a day by the mouth. | |
| 10/1/18. | Hæmoglobin ... ... | 70 per cent. |
| 22/1/18. | Hæmoglobin ... ... | 65 „ |
| 25/1/18. | Mist. arsen. tonic commenced. | |
| 4/2/18. | Hæmoglobin ... ... | 70 per cent. |
| 18/2/18. | Hæmoglobin ... ... | 72 „ |
| | Red blood corpuscles... | 3,120,000 per c.mm. |
| | Colour index ... ... | 1·14 |

*Final Result.*

Hæmoglobin improvement = 30 per cent.

Red blood corpuscle decrease = 380,000 per c.mm.

*Comments.*—(1) This patient suffered from a very heavy malignant tertian infection which was difficult to combat even with large doses of quinine. (2) The increase in the colour index from 0·6 to 1·14 is the feature most worthy of note. This is due to the decrease in the red blood corpuscle count with at the same time a considerable increase in the hæmoglobin percentage.

---

No. 7—Driver L. (galyl, one dose). No history of malaria. Admitted on November 16, 1917. Anæmic. Spleen, very much enlarged (3 inches below costal margin). *Blood film :* Malignant tertian gametocytes.

| | | |
|---|---|---|
| 30/11/17. | Hæmoglobin ... ... | 60 per cent. |
| | Red blood corpuscles... | 3,500,000 per c.mm. |
| | Colour index ... ... | 0·85 |
| 9/12/17. | Galyl 0·2 gramme intravenously. | |

| | | |
|---|---|---|
| 13/12/17. | Hæmoglobin ... ... | 74 per cent. |
| 3/1/18. | Hæmoglobin ... ... | 75 „ |
| | Red blood corpuscles... | 3,659,000 per c.mm. |
| | Colour index ... ... | 1·03 |
| 10/1/18. | Hæmoglobin ... ... | 90 per cent. |
| | Red blood corpuscles... | 4,800,000 per c.mm. |
| | Colour index ... ... | 0·94 |

*Final Result.*

Hæmoglobin improvement = 30 per cent.

Red blood corpuscle improvement = 1,300,000 per c.mm.

---

No. 8—Pte. M. E. (galyl and mist. arsenic tonic). History of malaria in August and September. Blood film : Small rings, probably malignant tertian. Admitted on November 9, 1917.

| | | |
|---|---|---|
| 30/11/17. | Hæmoglobin ... ... | 65 per cent. |
| | Red blood corpuscles... | 3,460,000 per c.mm. |
| | Colour index ... ... | 0·94 |
| 9/12/17. | Galyl 0·2 gramme intravenously. | |
| 13/12/17. | Hæmoglobin ... ... | 78 per cent. |
| 28/12/17. | Galyl 0·2 gramme intravenously. | |
| | From 23/12/17 to 6/1/18 patient had three relapses, and each time an additional 20 grains of quinine was given on the day of the rigor. | |
| 10/1/18. | Hæmoglobin ... ... | 80 per cent. |
| 18/1/18. | Slight relapse. | |
| 19/1/18. | Slight relapse. | |
| 22/1/18. | Hæmoglobin ... ... | 65 per cent. |
| 25/1/18. | Mist. arsen. tonic commenced. | |
| 27/1/18. | Hæmoglobin ... ... | 75 per cent. |
| 7/2/18. | Hæmoglobin ... ... | 84 „ |
| | Red blood corpuscles... | 4,140,000 per c.mm. |
| | Colour index ... ... | 1 |

*Final Result.*

Hæmoglobin improvement = 19 per cent.

Red blood corpuscle improvement = 680,000 per c.mm.

*Comments.*—When the rigor occurred the medical officer should have given this man a daily intramuscular or rectal quinine 20 grains, for a week, in addition to the 45 grains a day by mouth—this would have prevented the subsequent relapses.

---

No. 9—Staff-Sergt. R. Malaria, December, 1916, and in April, 1917, followed by dysentery. Admitted on December 7, 1917.

| | | |
|---|---|---|
| 14/12/17. | Hæmoglobin ... ... | 50 per cent. |
| 17/12/17. | Galyl 0·2 gramme intravenously. | |
| 19/12/17. | Hæmoglobin ... ... | 60 per cent. |
| 23/12/17. | Galyl 0·2 gramme intravenously, followed by a rise of temperature to 102° F. | |
| 3/1/18. | Hæmoglobin ... ... | 74 per cent. |
| 6/1/18. | Galyl 0·2 gramme intravenously, slight rise of temperature. | |
| 10/1/18. | Hæmoglobin ... ... | 77 per cent. |
| 15/1/18. | Hæmoglobin ... ... | 85 „ |
| | Red blood corpuscles... | 4,000,000 per c.mm. |
| | Colour index ... ... | 1·06. |
| 22/1/18. | Hæmoglobin ... ... | 82 per cent. |
| 25/1/18. | Mist. arsen. tonic commenced. | |
| 27/1/18. | Hæmoglobin ... ... | 72 per cent. |
| | Red blood corpuscles... | 3,350,000 per c.mm. |
| | Colour index ... ... | 1·07. |
| 20/2/18. | Hæmoglobin ... ... | 90 per cent. |
| | Red blood corpuscles... | 5,600,000 per c.mm. |
| | Colour index ... ... | 0·8. |

*Result after three doses of Galyl.*

Hæmoglobin improvement = 22 per cent.

Red blood corpuscle improvement = not known.

*Result after one course of Arsenic.*

Hæmoglobin improvement = 18 per cent.

Red blood corpuscle improvement = 2,250,000 per c.mm.

*Comments.*—(1) On rare occasions the temperature is found to react to the galyl, but the patient never appears to be any the worse for it. (2) Unfortunately a red count was not made before the first injection of galyl. (3) On admission patient was found to be very anæmic after attacks of malaria and dysentery. As he vomited arsenic by the mouth he was put on to a course of galyl, and reacted very well to this drug; later mist. arsenic tonic was again tried, this time with excellent results; the improvement between January 27, 1918, and February 19, 1918, being quite extraordinary.

---

CASES TREATED WITH MIST. ARSENIC TONIC: GRADUATED DOSES.

No. 1—Pte. E. Admitted January 5, 1918. Very anæmic. Spleen, much enlarged. *Blood film:* Malignant tertian gametocytes.

| | | |
|---|---|---|
| 10/1/18. | Hæmoglobin ... ... | 48 per cent. |
| | Red blood corpuscles... | 3,250,000 per c.mm |
| | Colour index ... ... | 0·74. |
| | Mist. arsenic tonic commenced (one course). | |
| 22/1/18. | Hæmoglobin ... ... | 58 per cent. |
| 7/2/18. | Hæmoglobin ... ... | 80 „ |
| | Red blood corpuscles... | 4,500,000 per c.mm. |
| | Colour index ... ... | 0·96. |

*Final Result.*

Hæmoglobin improvement = 32 per cent.

Red blood corpuscle improvement = 1,250,000 per c.mm.

No. 2—Private F. Admitted on December 27, 1917. Spleen plus.

| | | |
|---|---|---|
| 15/1/18. | Hæmoglobin ... ... | 60 per cent. |
| | Red blood corpuscles... | 3,656,000 per c.mm. |
| | Colour index ... ... | 0·8 |
| | Mist. arsenic tonic commenced (one course). | |
| 22/1/18. | Hæmoglobin ... ... | 70 per cent. |
| 4/2/18. | Hæmoglobin ... ... | 82 per cent. |
| 7/2/18. | Hæmoglobin ... ... | 82 per cent. |
| | Red blood corpuscles... | 4,500,000 per c.mm. |
| | Colour index ... ... | 0·91 |

*Final Result.*

Hæmoglobin improvement = 22 per cent.

Red blood corpuscle improvement = 844,000 per c.mm.

---

No. 3—Private W. Admitted January 5, 1918. Malaria six times; spleen plus and tender.

*Blood film:* Small rings, probably malignant tertian.

| | | |
|---|---|---|
| 15/1/17. | Hæmoglobin ... ... | 60 per cent. |
| | Red blood corpuscles... | 2,476,000 per c.mm. |
| | Colour index ... ... | 1·2 |
| | Mist. arsenic tonic commenced (one course). | |
| 22/1/18. | Hæmoglobin ... ... | 60 per cent. |
| 27/1/18. | Hæmoglobin ... ... | 64 per cent. |
| 4/2/18. | Hæmoglobin ... ... | 84 per cent. |
| 7/2/18. | Hæmoglobin ... ... | 84 per cent. |
| | Red blood corpuscles... | 3,930,000 per c.mm. |
| | Colour index ... ... | 1·07 |

*Final Result.*

Hæmoglobin improvement = 24 per cent.

Red blood corpuscle improvement = 1,454,000 per c.mm.

---

No. 4—Private C. Admitted January 5, 1918. Repeated severe attacks of malaria; rigor, and temperature 103·2° F. on January 9, 1918.

| | | |
|---|---|---|
| 15/1/18. | Hæmoglobin ... ... | 70 per cent. |
| | Red blood corpuscles... | 3,100,000 per c.mm. |
| | Colour index ... ... | 1·13 |
| | Mist. arsenic tonic commenced (one course.) | |
| 17/1/18. | Relapse; temperature 102° F. Additional 15 grains of quinine by mouth given. | |
| 18/1/18. | Evening: Rigor; temperature 104° F.; additional intramuscular quinine 20 grains. | |
| 22/1/18. | Hæmoglobin ... ... | 74 per cent. |
| 27/1/18. | Hæmoglobin ... ... | 68 per cent. |
| 4/2/18. | Hæmoglobin ... ... | 82 per cent. |
| 7/2/18. | Hæmoglobin ... ... | 82 per cent. |
| | Red blood corpuscles... | 4,240,000 per c.mm. |
| | Colour index ... ... | 0·98 |

*Final Result.*

Hæmoglobin improvement = 12 per cent.

Red blood corpuscle improvement = 1,140,000 per c.mm.

*Comments.*—The rigors somewhat affected the ultimate result. The second relapse should not have occurred; it was not enough to give 15 grains by the mouth when the cause of the rise of temperature was evidently due to the patient not absorbing the routine oral quinine (45 grains daily).

---

No. 5—Private R. Admitted January 8, 1918, as malaria recurrent,—malignant tertian; spleen, plus and tender.

*Blood film:* Malignant tertian trophozoites.

| | | |
|---|---|---|
| 15/1/18. | Hæmoglobin ... ... | 55 per cent. |
| | Red blood corpuscles... | 2,824,000 per c.mm. |
| | Colour index ... ... | 0·97 |

| | | |
|---|---|---|
| | Mist. arsenic tonic commenced (two courses). | |
| 22/1/18. | Hæmoglobin ... ... | 60 per cent. |
| 27/1/18. | Hæmoglobin ... ... | 60 per cent. |
| 31/1/18. | Second course of arsenic started. | |
| 4/2/18. | Hæmoglobin ... ... | 70 per cent. |
| 7/2/18. | Hæmoglobin ... ... | 70 per cent. |
| | Red blood corpuscles... | 4,070,000 per c.mm. |
| | Colour index ... ... | 0·92 |
| 18/2/18. | Hæmoglobin ... ... | 84 per cent. |
| | Red blood corpuscles... | 4,690,000 per c.mm. |
| | Colour index ... ... | 0·9 |

*Result of First Course.*

Hæmoglobin improvement = 15 per cent.

Red blood corpuscle improvement = 1,246,000 per c.mm.

*Result of Second Course.*

Hæmoglobin improvement = 14 per cent.

Red blood corpuscle improvement = 620,000 per c.mm.

*Final Result.*

Hæmoglobin improvement = 29 per cent.

Red blood corpuscle improvement = 1,866,000 per c.mm.

*Note.*—The great improvement in the blood constituents after the first course.

---

No. 6—Coy. Sergt.-Major W. Admitted January 9, 1918, with recurrent malaria; three previous attacks; markedly anæmic; spleen plus.

| | | |
|---|---|---|
| 15/1/18. | Hæmoglobin ... ... | 40 per cent. |
| | Red blood corpuscles... | 2,056,000 per c.mm. |
| | Colour index ... ... | 0·975 |
| 16/1/18. | Mist. arsenic tonic commenced (two courses). | |
| 22/1/18. | Hæmoglobin ... ... | 46 per cent. |
| 27/1/18. | Hæmoglobin ... ... | 52 per cent. |

| | | |
|---|---|---|
| | Red blood corpuscles... | 2,544,000 per c.mm. |
| | Colour index ... ... | 1 |
| 31/1/18. | Second course of arsenic started. | |
| 4/2/18. | Hæmoglobin ... ... | 74 per cent. |
| 7/2/18. | Hæmoglobin ... ... | 74 per cent. |
| | Red blood corpuscles .. | 4,240,000 per c.mm. |
| | Colour index ... ... | 0·87 |
| 18/2/18. | Hæmoglobin ... ... | 84 per cent. |
| | Red blood corpuscles... | 4,400,000 per c.mm. |
| | Colour index ... ... | 0·95 |

The two courses covered a period of thirty-two days. The gradual improvement during this time should be noted.

| | |
|---|---|
| On eleventh day hæmoglobin improvement ... ... ... ... ... | 12 per cent. |
| On eleventh day red blood corpuscle improvement ... ... ... ... | 488,000 |
| On twenty-first day hæmoglobin, a further increase of ... ... ... | 22 per cent. |
| On twenty-first day red blood corpuscles, a further increase of ... | 1,696,000 |
| On thirty-second day hæmoglobin, a still further increase of ... ... | 10 per cent. |
| On thirty-second day red blood corpuscles, a further increase of ... | 160,000 |

*Final Result.*

Hæmoglobin improvement = 44 per cent.

Red blood corpuscles improvement = 2,344,000 per c.mm.

Attention is called to improvement shown on the twenty-first day, five days after the completion of the first course.

As the arsenic becomes assimilated the hæmoglobin and red blood corpuscles improve fairly rapidly until a maximum point is reached.

During the second course the increase in both, although not so marked, is quite satisfactory.

Finally, it will be seen that both the hæmoglobin and red blood corpuscles in this case were doubled in the space of a month.

### Percentages of Hæmoglobin.

The following results are of additional assistance in arriving at an estimate of the value of mist. arsenic tonic in post-malarial anæmia.

All these cases took quinine 15 grains, t.d.s., by the mouth as well.

| Name | Before treatment | | After treatment. | | Increase |
|---|---|---|---|---|---|
| | | % | | % | % |
| Sergt. E.... | Hæmoglobin | 62 | Hæmoglobin | 80 | 18 |
| Pte. L. ... | ,, | 53 | ,, | 86 | 33 |
| Pte. T. ... | ,, | 58 | ,, | 78 | 20 |
| Sergt. C.... | ,, | 62 | ,, | 88 | 26 |
| Pte. S. ... | ,, | 80 | ,, | 95 | 15 |
| Pte. W. ... | ,, | 50 | ,, | 90 | 40 |
| Pte. J. ... | ,, | 70 | ,, | 84 | 14 |
| Pte. M. ... | ,, | 74 | ,, | 80 | 6 |
| Pte. B. ... | ,, | 72 | ,, | 86 | 14 |
| Pte. T. ... | ,, | 72 | ,, | 86 | 14 |
| Pte. H. ... | ,, | 62 | ,, | 76 | 14 |
| Pte. W. ... | ,, | 58 | ,, | 80 | 22 |
| Pte. B. .. | ,, | 28 | ,, | 75 | 47 |

*Conclusions.*—I have made a very careful estimation of the relative value of galyl and mist. arsenic tonic in these cases with the following results :—

*Average improvement on :—*

(a) *Galyl.*—One course = 2 doses.

Hæmoglobin percentage, an average increase of 33 per cent.

Red blood corpuscles, an average increase of 1,100,000 per c.mm.

(b) *Mist. Arsenic Tonic.*—One course.

Hæmoglobin percentage, an average increase of 25 per cent.

Red blood corpuscles, an average increase of 1,375,000 per cubic millimetre.

It is very evident from this that there is little or no difference in the results obtained from either method.

What mist. arsenic tonic loses in the matter of hæmoglobin percentage, it gains in the red blood corpuscle count.

There is, however, a considerable difference in the expense.

One course of galyl (0·4 grammes) costs 2s. 11d.

The cost of one full course of mist. arsenic tonic is exactly 2d., made up as follows :—

| | |
|---|---|
| Liq. arsenici hyd. ... ... | 1/32 penny. |
| Tinct. nucis vom. ... ... | 1/4 „ |
| Ferri et ammon. cit. ... ... | 1·9/16 „ |
| Aq. chlorof. ... ... ... | 5/32 „ |
| Total ... ... | 2d. |

If galyl had proved to be of much greater benefit to the individual than arsenic by the mouth, the question of cost would, of course, be of little or no consequence, but under the circumstances the cheapness of mist. arsenic tonic from the Army standpoint, and, what is of still greater importance, the simplicity with which it can be administered, makes the latter combination of drugs of infinitely more value in the treatment of malarial anæmia than intravenous galyl.

I now use galyl only in special cases :—

(1) If a patient's digestive system refuses to tolerate arsenic and iron by the mouth.

Staff-Sergeant R. (see Case 9, p. 150), is a case in point. This man vomited the mist. arsenic tonic, was given

three doses of galyl intravenously, and, although improvement in the hæmoglobin was not quite up to expectations, it improved his general condition, and laid the foundation for the extremely satisfactory results we obtained later when he was able to take the arsenic by mouth.

(2) In very severe post-malarial anæmia where the patient appears not to be able to absorb oral arsenic.

Private B. (see Case 3, p. 172), was a case of this sort. His hæmoglobin percentage only showed an increase of 2 per cent. after a full course of mist. arsenic tonic. Later, galyl two doses were tried with the following results :—

Hæmoglobin improvement = 40 per cent.

Red blood corpuscles improvement = 1,032,000 per c.mm.

He then did well on a second course of arsenic by the mouth. Fortunately cases such as these—requiring galyl—are comparatively rare.

*Note.*—In both methods of treatment, the hæmoglobin percentage appeared to shoot up rapidly while the increase in the red blood corpuscles manifested itself at a much later stage.

Another matter that should not be lost sight of is that all these anæmic patients were taking at least 45 grains of quinine a day to obviate further destruction of the red cells by the malaria parasites.

### Colour Index.

This, in post-malarial anæmia is almost invariably a low one. I calculated the average in sixteen cases before treatment with arsenic and found it to be 0·85. Only three of these had a colour index above the normal standard. This is important in view of what I have to say in regard to pernicious anæmia in the next chapter.

## CHAPTER IX.

## PERNICIOUS ANÆMIA AND MALARIA.

### Malarial Cachexia.

In order to facilitate the study of the group of cases, to which the term pernicious anæmia is usually applied, in its relation to the post-malarial variety of anæmia, and to enable the reader to grasp the salient points under discussion in this chapter, with the least possible effort on his part, I shall tabulate the blood changes associated with these conditions.

This should be of considerable use from a differential diagnostic standpoint.

Castellani and Chalmers, in their manual of *Tropical Medicine*, state "that according to Bignami, post-malarial anæmias are cases in which, in spite of the cessation of the malarial fever, the anæmia tends to progress. The anæmias are generally induced by age, malnutrition, overwork, pregnancy, nursing, &c., and are not due merely to the malarial infection. Bignami divides these into four types according to the characters of the blood."

### Tabulation of Blood Changes.

Ordinary Pernicious Anæmia. Prognosis — invariably fatal.

(*a*) Diminution of red corpuscles—may be less than half a million per c.mm.

(*b*) Diminution of hæmoglobin.

(*c*) *High colour index*, i.e., the amount of hæmoglobin in each corpuscle is often relatively greatly increased.

(*d*) Normoblasts, megaloblasts, microcytes and macrocytes found.

(*e*) Poikilocytosis (change in shape). Red cells may be tailed or crenated.

(*f*) Anisocytosis (variation in size). Some may be minute, others very large.

(*g*) Polychromatophilia (variation in staining qualities). The stain in many of the red cells being of a bluish tint.

(*h*) Some leucopenia.

POST-MALARIAL ANÆMIA (BIGNAMI'S CLASSIFICATION).

*First Type.*—Prognosis good.

(*a*) Diminution in erythrocytes (red cells) well marked.

(*b*) Colour index diminished.

(*c*) Normoblasts present.

(*d*) Leucopenia.

(*e*) Relative mononuclear increase.

*Second Type.*—Prognosis exceedingly bad.

(*a*) Great diminution in red cells.

(*b*) Normoblasts, megaloblasts and megalocytes.

(*c*) Poikilocytosis.

(*d*) Leucopenia.

(*e*) Relative mononuclear increase.

*Third Type.*—This is rapidly fatal. Similar in character to second type, but no normoblasts.

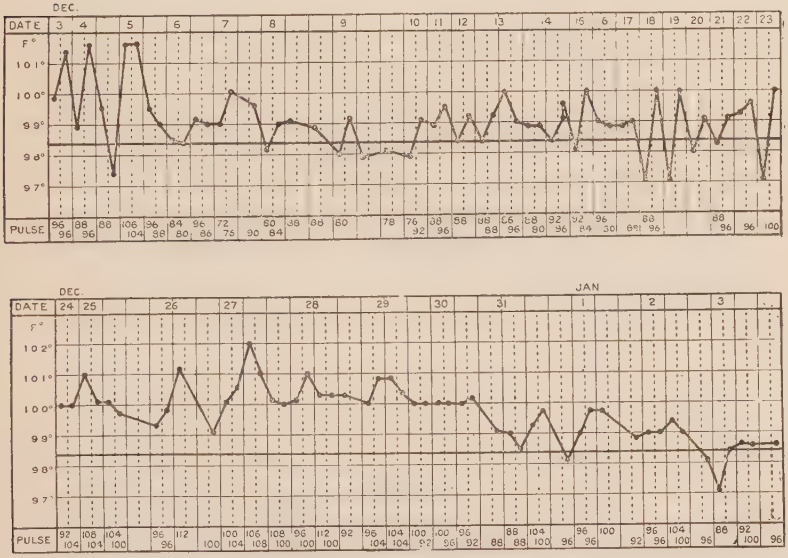
*Fourth Type.*—A grave chronic anæmia. Resembles the first type, but is specially characterized by: (*a*) Paucity of normoblasts; (*b*) Marked leucopenia.

*Note.*—THE LEUCOCYTES IN NORMAL BLOOD. Total count, about 7,000 per c.mm.

*Differential Count.*—Polymorphonuclears, 70 per cent.; small lymphocytes, 22 to 25 per cent.; large mononuclears, 2 to 4 per cent.; eosinophils, 2 to 4 per cent.; basophils, 0·5 per cent.; transitional cells, variable.

No. 1.—*Case of Profound Anæmia.*—Driver N., aged 43. Disease, profound anæmia. Admitted on December 3, 1917. In Balkans, 1 year 4 months. No history of malaria or other illness.

Onset of present illness, three weeks ago. General weakness; pain in limbs; shortness of breath; no shivering; no vomiting; no history of any hæmorrhage.




Case 1. Driver N.

*On admission.*—Temperature 99·8° F.; very anæmic; tongue clean and moist; pulse regular, good volume; carotid pulsation marked; heart, mitral systolic bruit with first sound, (?) aortic systolic murmur; spleen, just palpable, tender; no œdema; no ascites; urine normal.

*Blood film:* Marked anisocytosis; some poikilocytosis; no nucleated reds; parasites not found. Hæmoglobin, 26 per cent.; red blood corpuscles, 800,000; colour index, 1·6.

*Treatment*—Quinine, 15 grains, t.d.s.

3-5/12/17—Remittent temperature, 101° to 102° F. in evenings.

5/12/17—Galyl 0·2 grammes intravenously.

10/12/17—Hæmoglobin ... ... 30 per cent.

13/12/17—Galyl 0·2 grammes intravenously.

19/12/17—Hæmoglobin ... ... 33 per cent.

23/12/17—Patient seems weaker. Urine, slight trace of albumin.

25/12/17—Temperature 101° F.; vomiting.

10 a.m. Intramuscular quinine 20 grains.

6 p.m. Rectal saline with quinine, 30 grains; pulse weak, 104 per minute; strychnine $\frac{1}{30}$ grain, digitaline $\frac{1}{100}$ grain given.

26/12/17—Temperature 99·4° F.; pulse 96 and stronger; vomited once.

Evening. Temperature 101·2° F.

*Treatment*—Intravenous quinine 20 grains in normal saline 8 ounces; quinine 15 grains by mouth twice.

---

27/12/17—Temperature 100·4° F.; pulse 96; lemon yellow colour of skin becoming more marked.

*Blood film:* Marked poikilocytosis; polychromatophilia; leucopenia.

*Differential Leucocyte Count.*—Polymorphs, 64 per cent.; large mononuclears, 8 per cent.; small lymphocytes, 24 per cent.; transitional and degenerate cells, 4 per cent. Quinine stopped.

29/12/17—Temperature 100° F.; pulse 96.

1/1/18—Temperature normal; colour of skin rather worse; weakness increasing; occasional vomiting; heart, some dilatation.

---

5/1/18—Patient rather collapsed; pulse 100 per minute and feeble; respirations 36.

*Treatment*—Strychnine $\frac{1}{60}$ grain ; digitaline $\frac{1}{100}$ grain 4-hourly ; later, pituitrin 1 cubic centimetre.

---

6/1/18—Died at 2.15 a.m.

*Post-mortem Report.*—Brain : Extremely pale ; no hæmorrhages. Heart : Much dilated ; mitral orifice admits three fingers ; no valvular disease ; muscle extremely pale and atrophic. Lungs : Anæmic and areas of emphysema. Liver : Deeply bile-stained. Kidneys : Very anæmic. Spleen : Slightly enlarged and of a light purplish colour ; congested. All other organs extremely anæmic.

*Base Laboratory Report on Sections of Tissue.*—Spleen : No malarial pigment present; no nucleated red cells seen in splenic pulp. Supra-renals : Normal ; no melanin. Gland tissue : Normal ; no nucleated red cells seen ; no melanin.

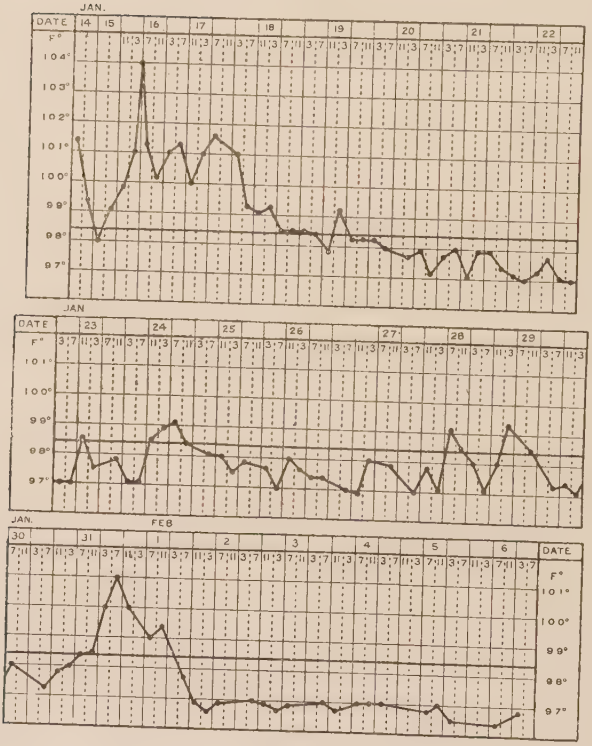
*Comments.*—The blood deficiency in this case is difficult to account for ; it resembles Bignami's third type. The complete absence of nucleated red corpuscles is inexplicable. The high colour index points to pernicious anæmia ; it was certainly not due to malaria.

---

No. 2. *Case of Pernicious Anæmia and Malaria.* Lance-Corporal G., aged 40 years. Admitted on November 13, 1917, with fracture of left tibia and fibula. No history of malaria or dysentery. Had occasional attacks of epistaxis in England before coming out.

14/1/18—Transferred to medical side. Temperature 101·4° F. ; pulse 120 per minute, regular ; very anæmic ; sallow ; tongue, clean and moist ; heart, mitral systolic bruit not conducted, double murmur in pulmonary

area, left border in nipple line; lungs, râles at both bases; spleen, much enlarged, 2½ inches below costal margin, firm, sharp edge, not tender; liver, much enlarged, lower border 1 inch above umbilicus, no tenderness.




Case 2. Lance-Corporal G.

*Blood film:* Poikilocytosis, anisocytosis, polychromatophilia. No parasites found. Hæmoglobin, 28 per cent.; red blood corpuscles, 1,320,000 per c.mm.; colour index, 1·06.

*Treatment*—Quinine 15 grains t.d.s.

15/1/18—Improvement. Temperature normal.

16/1/18—Galyl 0·2 gramme intravenously. Rigor one hour after injection, and temperature rose to 104° F. an hour later.

*Second blood film:* No parasites found.

Leucocyte count, total 3,000 per c.mm.

*Differential:* Polymorphs, 66·5 per cent.; mononuclears, 6·5 per cent.; lymphocytes, 20 per cent.; basophils, 3 per cent.; transitional cells, 4 per cent.

17/1/18—a.m. Had fairly good night; temperature 100° F. pulse 124, rather feeble; yellowish tinge of skin; abdomen, small amount of ascites—some dulness in both flanks; tongue furred.

5 p.m. Patient has vomited several times; vomit contains much bile; yellow tinge of skin becoming more marked; temperature 101° F.; pulse 120.

10 p.m. Urine clear amber colour; slight trace of albumin.

*Treatment—*

a.m. Strychnine and digitaline; rectal saline, 10 ounces, with brandy half ounce; intramuscular quinine, 20 grains.

5 p.m. Intravenous quinine, 20 grains in saline, 8 ounces.

10 p.m. Rectal saline with quinine, 20 grains, retained.

---

18/1/18—Patient seems better; temperature 99° F.; pulse 112; liver and spleen more enlarged and some increase of ascites; evening temperature 99; pulse 112.

*Treatment*—

9 a.m. Rectal saline with quinine, 20 grains.
12.30 p.m. Intramuscular quinine, 20 grains.
4.5 p.m. Rectal saline with quinine, 30 grains.

---

19/1/18 — Slight improvement; temperature normal; pulse 104; respirations 24.

Evening. General condition the same.

*Treatment*—

10 a.m. Rectal saline with quinine, 20 grains.
5 p.m. Intramuscular quinine, 20 grains.
9 p.m. Rectal saline with quinine, 30 grains, retained one hour and a half.

---

20/1/18—Patient passed mucus in stool, no blood; temperature 98° F.; pulse 96.

Evening. Stool still contains mucus.

*Treatment*—

10 a.m. Rectal saline with quinine, 20 grains.
4.30 p.m. Intramuscular quinine, 20 grains.
10 p.m. Rectal saline with quinine, 20 grains.

---

21/1/18—a.m. Temperature 97·4° F.; pulse 92. Abdomen; liver, size about the same; spleen has diminished about three-quarters of an inch in the last three days.

Evening. Condition same.

*Treatment*—

a.m. Intramuscular quinine, 20 grains.
p.m. Intramuscular quinine, 20 grains.

---

22/1/18—Patient taking nourishment better; no vomiting; general condition about the same; tongue still rather dry.

Evening. Temperature 98° F.; pulse 92 per minute.

*Treatment*—

11 a.m. Rectal saline with quinine, 20 grains.

6 p.m. Intramuscular quinine, 20 grains.

---

23/1/18—Patient rather drowsy.

*Treatment*—

a.m. Rectal saline with quinine, 30 grains.

6 p.m. Intramuscular quinine, 20 grains.

10 p.m. Rectal saline with quinine, 30 grains.

---

24/1/18—Patient brighter this morning; temperature normal; pulse 92.

*Blood film* shows marked anisocytosis with poikilocytosis and polychromatophilia; no nucleated red cells seen; parasites not found.

*Treatment*—

a.m. Rectal saline with quinine, 30 grains.

6 p.m. Intramuscular quinine, 20 grains.

10 p.m. Rectal saline with quinine, 30 grains.

---

25/1/18—Patient still very anæmic.

*Treatment*—Rectal saline with quinine, 30 grains; intramuscular quinine, 20 grains.

---

26/1/18—Patient not improving; some œdema about ankles; no diminution in size of liver, but spleen slightly less.

*Treatment*—

a.m. Rectal saline with quinine, 30 grains.

p.m. Intramuscular quinine, 20 grains.

---

27/1/18—Patient not so well; seems weak; yellow tinge of skin; marked subcutaneous œdema more or less general over whole body; quinine stopped; mist. arsenic tonic, graduated doses commenced.

28/1/18—Urine: Quantity passed in last twenty-four hours, 61 ounces; greenish brown colour; no albumin.

Seen by Assistant Consulting Physician, who suggested that administration of galyl *per rectum* might be tried as it had been found impossible to give patient intravenous injections without cutting down on the superficial veins.

Evening. Temperature 99·2° F.

*Treatment*—Galyl 0·175 gramme in saline *per rectum*.

---

29/1/18—Had restless night; temperature 98°; pulse 96; respirations 20.

*Blood films:* Poikilocytosis, anisocytosis, megaloblasts, normoblasts, megalocytes. Hæmoglobin, 16 per cent.; red blood corpuscles, 927,000 per c.mm.; colour index, 0·87.

Evening. More œdema at bases.

*Treatment*—Galyl 4·4 c.gramme by mouth as patient cannot retain it by rectum.

---

30/1/18—Condition about the same.

10 a.m. Galyl 4·4 c.gramme by mouth.

Seen by Assisting Consulting Surgeon with reference to possibility of a direct blood transfusion. A donor, the Company Sergeant-Major of the hospital, was chosen, and his blood tested with the patient's blood and found not to be hæmolytic or agglutinative.

9.30 p.m. Blood transfusion done, about 8 ounces of blood passed into patient's circulation after considerable difficulty in finding a

suitable vein on account of the general œdema and the smallness of the vessels. Patient's pulse improved after the operation.

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31/1/18—*Blood Examination.*—Hæmoglobin, 20 per cent.; red blood corpuscles, 700,000 per c.mm.

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1/2/18—Condition same. Evening temperature, 101° F.; pulse 100; respirations 24.

---

2/2/18—Patient seems weaker and more sleepy. Temperature 97° F.; pulse 92. The Acting Officer-in-Command Surgical Division was called in with a view to another transfusion of blood, but considered it inexpedient.

---

4/2/18—Temperature keeps subnormal; pulse 92. Patient much weaker and more drowsy; œdema increasing. Anæmia becoming more marked. *Skin has a marked greenish yellow tinge.*

10.30 p.m. Had a syncopal attack and was unconscious for about ten minutes, but later rallied a little.

---

5/2/18—Much weaker and practically unconscious all day.

---

6/2/18—Died at 8 a.m.

---

*Post-mortem Report.*—The body was of a marked lemon yellow colour.

Brain: Extremely anæmic.

Heart: Muscle pale and slightly atrophic. Chambers dilated. Valves normal.

Lungs: Œdematous.

Liver: Much enlarged, firm, and of a peculiar russet-brown colour, wtth areas of venous congestion.

Spleen: Enlarged to about five times normal size, firm, and of a crushed strawberry colour. The spleen was different coloured from that in malaria.

Kidneys: Pale in colour. The larger cortical and medullary vessels were congested, and stood out prominently.

Supra-renals.—Much enlarged.

No other macroscopic change. The post-mortem appearance strongly suggested death from pernicious anæmia. There was œdema of both legs.

*Base Laboratory Report.*—Liver: Areas of hæmorrhages and necrosis throughout liver affecting portion around central veins of lobules. Fatty changes present. Free iron present. No melanin seen.

Spleen: Very dilated and full of blood. Malpighian bodies; no change.

Adrenals: Degeneration of fibrous tissue. Hæmorrhages present in tissue.

Kidneys: Degeneration of renal epithelium present—marked in convoluted tubules. Some of the glomeruli fibrosed. Kidney vessels thickened. Free iron present, and debris in tubules.

*Comments.*—Because there was no history of malaria, and no parasites were found in the blood films, this case was diagnosed simply as "anæmia," but, on account of the enlargement of the spleen and liver and the intense anæmia, I looked upon it as a pernicious anæmia in a malarial subject.

The blood picture tallied in every respect with per-

nicious anæmia, except that the colour index was low, and the leucopenia more marked than in ordinary "pernicious."

It resembled the second type of post-malarial anæmia, described by Bignami, in the very marked leucopenia and the presence of a relative mononuclear increase. The blood condition also fitted in with Bignami's fourth type (a grave chronic anæmia), in which marked leucopenia is the principal feature.

Post-mortem, it appeared to be a case of pernicious anæmia, except that the spleen was enlarged, but instead of the dark chocolate colour usually found after death from malaria, the spleen was of a crushed strawberry colour; this was probably due to the deposition of iron pigment.

I do not consider that these cases are anæmias secondary to malaria. I incline to the opinion that they are pernicious anæmias in patients suffering from chronic malaria as well.

The low colour index and the marked leucopenia are easily explained by the malaria. The colour index is invariably low in the anæmia which occurs in malaria, and it is reasonable to suppose that a case of pernicious anæmia with chronic malaria super-added would not necessarily have a high colour index, and that the leucopenia would be more evident than usual.

In all the cases of malarial anæmia I have treated, I have never found normoblasts or megaloblasts in the blood. The blood films of the worst case of this kind Private B. (see Case 3, p. 172) showed "anisocytosis (marked), poikilocytosis, but no normoblasts, megalocytes or megaloblasts."

The hæmoglobin was 20 per cent.; red blood corpuscles, 1,792,000 per c.mm.; colour index, 0·8.

This condition on treatment with quinine 15 grains t.d.s., and courses of galyl and arsenic by mouth improved in two months to: Hæmoglobin, 74 per cent.; red blood corpuscles, 3,560,000 per c.mm.; colour index, 1·05.

Lance-Corporal C. received treatment by these drugs as well, but never showed the slightest improvement, due, I consider, to the fact that he was suffering from pernicious anæmia as well.

As cacodylate of soda was not available, and it was an impossibility to give intravenous galyl without undertaking an extensive dissection to find a vein in the œdematous subcutaneous tissue, galyl per rectum and by the mouth had to be resorted to. The effects, however, were negligible.

Although the assistant consulting physician stated that in his opinion the post-mortem diagnosis of pernicious anæmia was very doubtful because of the rapid history, persistent low colour index and enlarged spleen, still I consider that this was a case of pernicious anæmia which became progressively worse in a very short time on account of a super-added malarial infection.

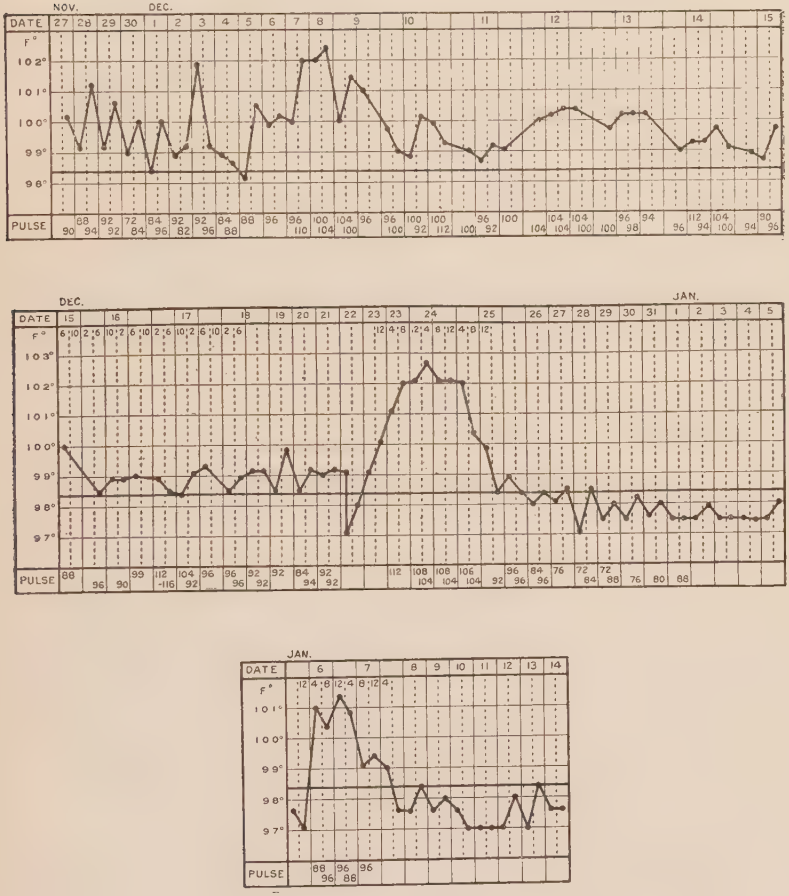
---

The notes of the next case, an extremely intense anæmia, are of very great interest because of the way the patient recovered on galyl treatment.

Private B. was first put on to arsenic by mouth, but as he made very little improvement, he was given galyl intravenously with the following satisfactory result:—

Case 3.—*Post-Malarial Anæmia.* Private B., aged 20. Admitted on November 27, 1917. In Balkans 11 months. Malaria six times, twice in hospital, mild attack about a month ago. Has been unwell for three weeks, complains of general weakness. This had become progressive,

and slightest walk causes much exhaustion. Is very dyspnœic and extremely anæmic. Skin, dead white pallor.




Case 3. Private B.

*On admission.*—Tongue clean; spleen enlarged; heart normal size; systolic murmurs, in mitral and aortic areas —hæmic; dyspnœa; frequency of micturition; no

œdema of ankles or face; temperature 100° F., pulse 90.
*Treatment*—Quinine 15 grains, t.d.s. Mist. ferri arsen.

---

3/12/17—Patient extremely anæmic.

*Blood Examination.*—Hæmoglobin, 20 per cent.; red blood corpuscles, 1,792,000 per c.mm.; colour index, 0·8.

*Blood film:* Parasites not found. Marked anisocytosis, also poikilocytosis. Has had mild epistaxis occasionally.

---

*Treatment*—

4/12/17. Mist. arsenic tonic in graduated doses, as well as quinine 45 grains daily.

---

7/12/17—Evening: Temperature rose to 102° F.; patient quite comfortable; tongue clean and moist.

8/12/17—Temperature still 102° F.; evening temperature 102·4° F.; heart, marked systolic in mitral and aortic regions; also pulmonary bruit. No dilatation; no pericardial friction; throat, pharyngeal congestion on left side; spleen enlarged and tender; liver, no enlargement or tenderness; has vomited and has a dry cough.

a.m. Intramuscular quinine 20 grains.

p.m. Rectal saline with quinine 20 grains.

10/12/17—Temperature 99° F. Seen by Colonel Purves Stewart, Consulting Physician, who recorded splenic enlargement 1½ inches below costal margin.

19/12/17—Temperature remaining normal.
Hæmoglobin, 22 per cent. An improvement of only 2 per cent. in the hæmoglobin on a full course of mist. arsenic tonic.

23/12/17—11 a.m. Galyl 0·2 gramme intravenously. Temperature rose steadily after the injection to 102° F. at 8 p.m. Patient quite comfortable; slight headache; pulse 108, good. Mist. diaphoretic 1 ounce.

24/12/17—a.m. Temperature 102° F.; pulse 108.
8 p.m. Temperature falling, 100·4° F.

*Blood film:* Negative.

25/12/17—Temperature normal. Patient much better.

27/12/17—Hæmoglobin, 25 per cent.

30/12/17—"Up" for one hour.

3/1/18—Hæmoglobin, 42 per cent.

6/1/18—Galyl 0·2 gramme intravenously. Reaction not quite so marked as after previous dose. Temperature 101·2° F., but fell to normal in eight hours.

8/1/18—Patient doing well; temperature normal.

10/1/18—Hæmoglobin, 48 per cent.

15/1/18—Quinine reduced to 10 grains, t.d.s. Hæmoglobin, 58 per cent.; Red blood corpuscles, 2,610,000; Colour index 1·1.

22/1/18—Hæmoglobin, 60 per cent. Patient was at this stage again treated with mist. arsen. tonic in graduated doses.

27/1/18—Hæmoglobin, 62 per cent.; red blood corpuscles, 2,824,000; colour index, 1·1.

4/2/18—Hæmoglobin, 70 per cent.

7/2/18—Hæmoglobin, 70 per cent.; red blood corpuscles, 3,840,000; colour index, 0·92.

18/2/18—Hæmoglobin, 74 per cent.; red blood corpuscles, 3,560,000; colour index, 1·05.

*Comments.*—The improvement on galyl should be noted as it is one of a type of case in which this drug may be used with advantage.

The failure of arsenic by mouth in the first instance is probably due to the weakened digestive organs of the patient not being able to assimilate the arsenic.

A comparison with the two preceding cases is very interesting notwithstanding the fact that there was very little difference in the degree of anæmia in any of these three cases.

Case 3, Private B., was the only one who recovered. His was a real post-malarial anæmia and yielded to the quinine and arsenic.

The quinine prevented the breaking down of the red cells while the arsenic assisted in building up other corpuscles.

These drugs have been shown to be useless in the profound anæmias generally known as "pernicious anæmias," although when the latter conditions are complicated by malaria, quinine and arsenic may cause a temporary improvement.

MALARIAL CACHEXIA is an advanced stage of malarial anæmia with great enlargement of the spleen and liver, fluid in the flanks and œdema about the feet and ankles.

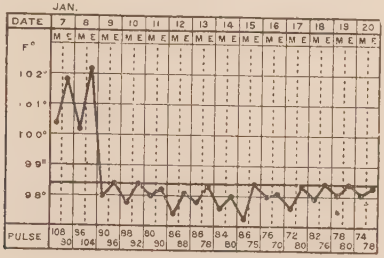
*Treatment*—Quinine and arsenic.

CASE 1.—Pte. O., aged 35. Service, 2 years 10 months. Admitted January 7, 1918. In Balkans, 1 year 4 months. Malaria in October, 1915, and five relapses since. No dysentery. Has been unfit for duty since return from convalescent camp on December 6, 1917.

*Onset of present illness—*

*Symptoms.*—Pains in head and chest; no vomiting; no diarrhœa; epistaxis from left nostril for about five hours; cough in mornings.

*On admission.* Temperature 100·2° F.; pulse 108; tongue, clean; heart, mitral systolic; lungs, normal; abdomen distended; liver, 1½ inches below costal margin, tender; spleen, 1¼ inches below costal margin, tender; dulness in flanks varies about half an inch with change of position. Transmitted wave on percussion. Evening temperature rose to 101·8° F.; pulse 90.




Case 1. Private O.

*Treatment.*—Calomel and mag. sulph.; quinine sulph. 15 grains t.i.d.

8/1/18—a.m. Temperature 100·2°F.; pulse 96.
p.m. Temperature 102·4°F.; pulse 104.

9/1/18—Temperature fell to normal and remained so.

14/1/18—Seen by Assistant Consulting Physician who recommended daily examination of stools for amœbæ of dysentery; result negative.

16/1/18—Leucocyte count 3,600 per cubic millimetre.

17/1/18—Spleen and liver, no change; dulness in flanks slightly less.

*Treatment.*—Quinine, 15 grains, t.d.s. by mouth continued, and in addition intramuscular quinine, 20 grains, given daily for the next four days.

---

19/1/18—Hæmoglobin, 60 per cent.

21/1/18—Splenic dulness decreased about 1 inch; liver dulness decreased about three-quarters of an inch.

*Treatment.*—Intramuscular quinine, 20 grains; rectal saline with quinine, 20 grains, t.d.s.; oral quinine stopped.

---

22/1/18—Improvement continuing; rectal salines with quinine, 20 grains, t.d.s., given for the next four days.

26/1/18—Spleen now only just palpable; liver, in mid-clavicular line, just reaches costal margin; dulness in flanks entirely gone.

29/1/18—Patient improved and is a much better colour.

*Treatment.*—Rectal salines with quinine, 20 grains, continued.

---

5/2/18—Patient states he feels much better; taking food well; no abdominal pain; rectal salines stopped; quinine, 15 grains, t.d.s., by mouth.

11/2/18—Patient "up."

1/3/18—Patient shows marked progress; spleen and liver normal; no anæmia; quinine reduced to 10 grains, t.d.s.

*Résumé of Quinine Treatment from January 7 to March 7, 1918.*

| | | |
|---|---|---|
| Quinine, 45 grains, daily for 10 days | ... | = 450 grains |
| Quinine, 65 grains, daily for 4 days | ... | = 260 grains |
| Quinine, 70 grains, daily for 15 days | ... | = 1,050 grains |
| Quinine, 45 grains, daily for 24 days | ... | = 1,080 grains |
| Quinine, 30 grains, daily for 7 days | ... | = 210 grains |
| Total amount in 2 months | ... | 3,050 grains |
| Daily average ... ... ... | | 50 grains |

*Comments.*—(1) The improvement in the condition of the patient between January 17 and January 26, 1918, when he was vigorously treated with quinine intramuscularly and by the rectum (average 60 grains a day), is very definite.

(2) This condition is fairly frequently met with in malarial subjects and the treatment should be carefully noted.

(3) The appearance of complete healthiness which this patient showed on the day he was discharged from hospital was a visible and veritable triumph for quinine, which, by preventing relapses and the consequent blood destruction, allowed his natural powers of recuperation to overcome the anæmia without any assistance from artificial blood tonics such as iron and arsenic.

## CHAPTER X.

## BLACKWATER FEVER.

THIS is a name commonly, but erroneously, given to a complication of malaria in which hæmoglobin appears in the urine.

Hæmoglobinuria may be classified into :—

(*a*) *Malarial Hæmoglobinuria.*—An early stage of blackwater fever in which the urine is of a strawberry colour containing hæmoglobin, but little or no debris, epithelial cells or casts. The urine clears up rapidly on quinine. This variety I have termed "red water fever."

(*b*) *Quinine Hæmoglobinuria.*—A transitory condition occurring in patients who have an idiosyncrasy towards quinine in the same way as the drug may cause a rash or amblyopia. The treatment is to stop the quinine at once and give plenty of fluids.

TRUE BLACKWATER FEVER.—The above conditions must be distinguished carefully from genuine blackwater fever, which is a very serious phase of malaria associated with jaundice, vomiting of greenish fluid, and a dirty yellowish, furred tongue. The spleen and liver are enlarged and tender, and the urine at the height of the attack, is of a dark, almost black porter colour. On standing, a quantity of chocolate brown debris with a tinge of red in it, is deposited, the supernatant fluid becoming lighter in shade. As the condition clears up, the fresh urine also becomes less dark, the colour graduating through reddish brown to orange, and finally to the ordinary light straw tint of normal urine, the process

occupying about forty-eight hours. The debris consists of broken-down red blood corpuscles, epithelial cells, and granular and epithelial casts.

*Blackwater fever* is thus an acute general toxæmia chiefly affecting the kidneys.

The malaria toxins cause fatty degeneration of the epithelium of the convoluted tubules, which strips off and, together with altered blood cells and hæmoglobin, forms a granular material. This debris is found principally in the lumen of the lower part of the convoluted tubules—where the toxins are excreted, and causes a mechanical blockage there.

Unless the condition is rigorously treated with quinine in the early stages the damage to the epithelium is so great that suppression of urine may supervene. Suppression is due to the filling of the convoluted tubules with debris. The pressure between the blockage and the glomeruli becomes greater than the pressure in the circulation above, with the result that the secretory cells of the glomeruli cease to act ; thus we do not find much swelling of the kidneys, a condition which it would be reasonable to expect if a blockage occurred in the convoluted tubules, and the cells of the glomeruli *continued* to secrete urine. It will be seen from this that in treating a case it is essential to increase the pressure in the systemic circulation as much as possible, so as to overcome the obstruction in the lower part of the convoluted tubules and allow the cells which secrete urine to perform their functions normally. The successful accomplishment of this is the probable explanation of the excessive passage of urine after a partial suppression. It is evident therefore that the earlier, and the more vigorously, a case is treated, the better the prognosis will be. Intravenous injections (with quinine) are best

for this purpose and the alkaline gum solution of Bayliss may be used instead of normal saline. Although the pulse improves temporarily after an injection of 8 or 10 ounces of normal saline, the latter is excreted so rapidly by the skin that the increased pressure in the circulation is not maintained. Saline, however, acts beneficially by eliminating the toxins which are destroying and paralysing the kidney cells.

On microscopical examination of sections of the kidney the epithelium of the convoluted tubules may be found to be in an advanced stage of degeneration, the lumen of the tubules being packed with debris, while in the same field perfectly normal tubules may be seen. These normal tubules seem to indicate that the toxins have paralysed the cells without destroying them.

*Ætiology.*—Different schools hold different opinions as to the ætiology of blackwater fever, and various theories have been advanced to explain it.

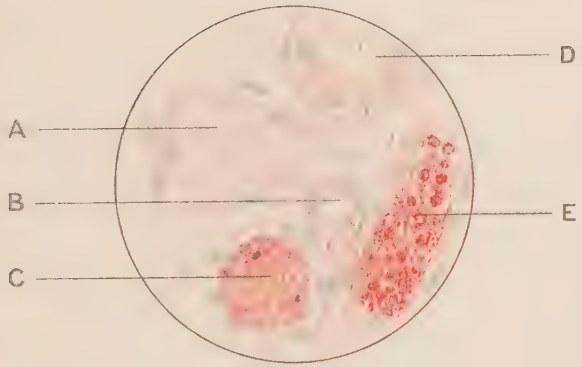
Malaria, quinine and an unknown agent are the most popular causes assigned.

In my opinion, the condition is due to the neglect of one of the elementary principles of medicine, neglect to counteract the effects of the malarial parasites and its toxins by quinine.

In other words, blackwater fever is a result that may be expected in pernicious malarial fever which has been allowed to relapse frequently and has not been adequately treated with quinine.

The disease occurs only in malarial countries and in malarial subjects, and it appears to me that other theories for its causation although highly interesting from an academic standpoint, are of little practical value, and are likely to do harm inasmuch as, according to them, quinine is contraindicated in the treatment of the condition.

Section of Kidney in a Case of Blackwater Fever.




A.—Distended and degenerate 1st convoluted tubule with cast-off cells and debris in lumen.

B.—A normal 2nd convoluted tubule.

C.—A distended 2nd convoluted tubule with blood cells, debris and pigment.

D.—Longitudinal section of 2nd convoluted tubule packed with debris and red cells.

E.—A more or less normal 1st convoluted tubule.

Hæmatoxylin and Eosin. x 350.

*To face p.* 182

*Predisposing Causes.*—(1) Cold; (2) fatigue.

These lower the vitality of persons whose powers of resistance have already been greatly reduced by the action of the malarial poisons.

A perusal of the notes in the following cases will throw a good deal of light on the subject.

*Statistics for the last Four Months.*

| | Number of cases | Deaths |
|---|---|---|
| Malarial hæmoglobinuria ... | 5 ... | *Nil* |
| Blackwater fever ... ... | 17 ... | 2 |

Case 1. *Blackwater Fever and Quinine Amblyopia.*—Sergeant M., aged 24. Service, 2 years 6 months. Admitted on December 22, 1917. In Balkans, 1 year 3 months.

*Previous History.*—Malaria in July, 1917. Numerous minor attacks, but none for a month.

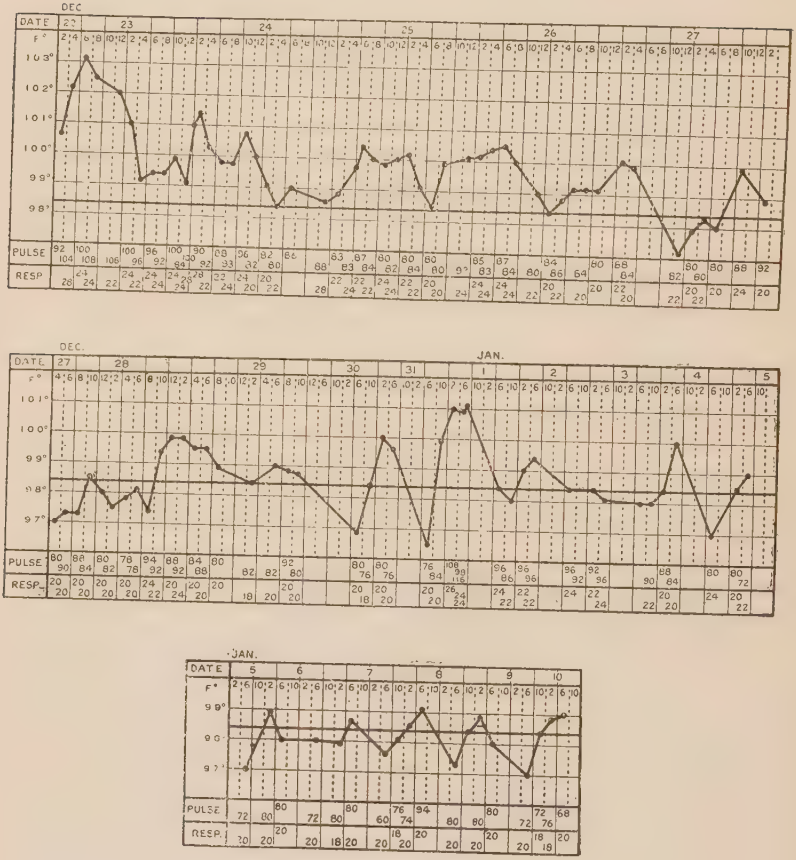
*Onset of present illness:*—Yesterday (December 21, 1917).

*Symptoms.*—Shivering, sweating, headache; no vomiting; passed urine early this morning mixed with blood; slight discomfort, but no actual pain on micturition.

*On admission.* Temperature 97·6° F.; pulse 92; urine very dark in colour.

3.30 p.m. Temperature 102·2° F.; pulse 104; respirations 28; skin and conjunctivæ jaundiced; tongue dirty, white fur; heart and lungs normal; spleen, plus and tender; liver, 1 inch below costal margin, slightly tender; bladder, marked tenderness; slide taken; urine sent for examination.

*Treatment.*—Calomel, 5 grains; intramuscular quinine, 20 grains; quinine sulph, 15 grains, by mouth.




Case 1. Sergeant M.

4.30 p.m. Seen by Colonel Sir Ronald Ross and the Officer-in-Charge of Medical Division. Sir Ronald Ross recommended that no quinine be given, and advised sod. bicarb. 15 grains, in hot water every hour and plenty of hot fluids. On seeing urine he gave a bad prognosis, and stated that in his opinion patient would

be dead in three days, and that, according to Koch, the giving of quinine would produce a greater hæmolysis.

6 p.m. Temperature 103·2° F.; pulse 100; respirations 24; vomited yellow bilious fluid.

11 p.m. Retches frequently, and then has no control of bowels.

---

23/12/17—Vomited freely during night; did not retain fluids; urine, 17 ounces, no change; rectal saline retained.

8.50 a.m. Temperature 99·6° F.; pulse 92; respirations 24; jaundice much more marked; tongue foul; headache.

11.30 a.m. *Blood film:* Malignant tertian rings; marked mononuclear increase. Urine: Faintly alkaline; specific gravity, 1,023; very dark red; large amount of hæmoglobin. Bacteriological report on debris: Abundant broken-down red blood corpuscles, scanty whole red blood corpuscles, epithelial and granular casts, numerous large epithelial cells, and masses of epithelium. The Officer-in-Charge of Medical Division instructed that intravenous and intramuscular injections, totalling 80 grains of quinine, be given within the next twelve hours. Patient had a slight rigor after first intravenous. Urine, dark port-wine colour.

6 p.m. Temperature 99·8° F.; pulse 88; respirations 22; vomited some bilious-looking fluid; says he feels a little better; urine light port-wine colour. Microscopical

report on urine: Some red blood corpuscles; large amount of debris of red blood corpuscles; large number of degenerated renal epithelial cells; granular casts and stellate phosphates.

10 p.m. Temperature 100·6° F.; pulse 96; respirations 24; tongue very dirty; passed urine, 12 ounces, light strawberry colour.

*Treatment.*—

11.45 a.m. Intravenous quinine, 20 grains, in saline, 8 ounces.

6 p.m. Intravenous quinine, 20 grains, in saline, 8 ounces.

10 p.m. Intravenous quinine, 20 grains, in saline, 8 ounces; intramuscular quinine, 20 grains.

24/12/17—Vomited frequently during the night (bilious).

6 p.m. Pituitrin 1 c.c.

7 a.m. Informed sister he could not see. Pupils were widely dilated; reacted to strong light (electric torch) and immediately dilated again.

9 a.m. Examined by Officer-in-Command of Medical Division who found that patient was totally blind.

10.15 a.m. Seen by Hospital Ophthalmologist who reported as follows: "Examination—Patient has absolutely no perception of light with either eye, even when tested with an electric torch held a few inches in front of eyes. Pupils (right and left) semi-dilated; reaction to light—with strong light pupils immediately contract

and then immediately dilate. Ophthalmoscopic examination: Both discs appear slightly pale, but pallor is not definitely abnormal. Vessels (both arteries and veins) normal in size. No other abnormal condition detected by ophthalmoscope."

11.15 a.m. Told the matron he could see the outline of the windows on the opposite side of the ward.

1.50 p.m. Able to see the roof of next hut and count fingers.

4 p.m. Could describe the appearance of another patient, colour of moustache, &c. Noticed that he had no badge on his cap.

5 p.m. Seen by the Consulting Ophthalmologist of the Salonika Command who made the following notes: "Seen in bed. Pupils small, equal, contract fairly readily to light. Refraction, right and left, a considerable degree of hypermetropia. Ophthalmoscope, each eye, retinal arteries of normal size; optic discs have a good colour. Right vision: Counts fingers readily at 4 feet. Left vision: Counts fingers at 2 feet; both without glasses. Fields of vision tested with hands show definite contraction.

6 p.m. Temperature 100° F.; pulse 87; respirations 22. Mental condition more alert.

Microscopical report on urine passed this morning (December 24, 1917): Specimen not so deeply coloured. Casts and epithelial cells still present but in smaller quantities.

*Second blood film:* Very scanty malignant tertian parasites.

*Treatment.*—Rectal salines, 4-hourly. Plenty of fluids by mouth. Strychnine $\frac{1}{60}$ grain; digitalin $\frac{1}{100}$ grain, 4-hourly; no quinine.

---

25/12/17— a.m. Only vomited once in night; tongue, white, furred, but moist. Photographed in ward. Urine in twenty-four hours = 88 ounces. Losing red colour and becoming much yellower. Deposit: brownish-coloured debris, above which a light flocculent layer, with a clear amber-coloured fluid on top. Jaundice slightly less marked. Says he feels better.

8 p.m. Temperature 99·8° F.; pulse 60; respirations 20. Slight headache. Took great interest in Christmas festivities during the afternoon. Jaundice less marked.

*Treatment.*—Rectal salines and strychnine $\frac{1}{60}$ grain, 4-hourly continued. No quinine on account of the attack of amblyopia.

---

26/12/17—Much better night; no vomiting. Urine in twenty-four hours = 59½ ounces, dark straw colour.

2 p.m. Temperature 100·2° F.; pulse 88; respirations 20.

*Treatment.*—Intramuscular quinine 20 grains, calomel 5 grains; quinine was resumed at this stage on account of the rise of temperature, and because the patient's vision had become quite normal.

8 p.m. Temperature and pulse normal.

Report on urine (December 26, 1917). Scanty epithelial cells from urinary tract, certain of which are degenerate. Debris of granular nature.

---

27/12/17—Conjunctivæ still jaundiced; temperature 99·8°F.

*Third blood film:* Parasites not found. Polychromatophilia.

Urine in twenty-four hours = 73 ounces, light straw colour.

4 p.m. Vomited once during the afternoon. Patient weak but improving. Eyesight quite normal.

*Treatment*—11 a.m. Intramuscular quinine 20 grains; quinine sulph. 15 grains, t.d.s.

---

28/12/17—Very good night; no vomiting. Urine in twenty-four hours = 67 ounces, normal colour.

10 a.m. Temperature 99·8° F.; pulse 92; respirations 22. A very faint mitral systolic murmur; spleen plus and tender.

*Treatment.*—Intramuscular quinine 10 grains; quinine sulph. 15 grains, t.d.s.

---

29/12/17—Colour improved. Urine in twenty-four hours = 42½ ounces.

*Treatment.*—Quinine sulph. 15 grains, t.d.s.

---

30/12/17— a.m. Eyesight good; field of vision tested with hands now normal; feels very well. Urine in twenty-four hours = 33 ounces.

Afternoon Temperature 100° F.; pulse 80; respirations 20; bowels constipated.

*Treatment.*—Calomel 5 grains; quinine sulph. 15 grains, t.d.s.

31/12/17—Temperature 97° F.; pulse 76; respirations 20; still very sallow; bowels acting. Urine in twenty-four hours = 37½ ounces; heavy deposit of urates.

10 a.m. Temperature 101° F.

11 a.m. Urine, very dark port-wine colour again, a large quantity of hæmoglobin; patient looks very pale; tongue dirty.

6 p.m. Temperature 100·8° F.; vomited once during intravenous injection.

*Fourth blood film:* Parasites not found.

Report on urine: Large amount of granular deposit; broken-down red blood corpuscles; very scanty normal red blood corpuscles; several large epithelial cells; certain number of degenerated renal cells.

*Treatment.*—Quinine, 15 grains, t.d.s.

11 a.m. Intramuscular quinine, 20 grains.

6 p.m. Intravenous quinine, 20 grains.

---

1/1/18—Urine lighter in colour, 39½ ounces in twenty-four hours.

*Treatment.*—Quinine, 15 grains, t.d.s.

12 noon. Intramuscular quinine, 20 grains.

10 p.m. Rectal quinine, 20 grains, in saline, 10 ounces.

---

2/1/18—Temperature 98·4° F.; pulse 96; respirations 24; urine much clearer, 49 ounces in twenty-four hours; sight has not been affected in the slightest degree by the quinine taken since his relapse.

*Treatment.*—Quinine, 15 grains, t.d.s.

12 noon. Intramuscular quinine, 20 grains.

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3/1/18—Still improving; urine dark yellow with quantity of urates; no blood.

CASE 1.—Sergeant M. Blackwater fever and quinine amblyopia. Taken on Christmas Day, 1917, eighteen hours after he had recovered his sight.

Medical Officer giving an intramuscular injection to Case 2, Private E., blackwater fever, assisted by Case 1, Sergeant M. who had just recovered from the same condition.

6 p.m. Temperature 100° F.; urine normal; patient looks better.

*Treatment.*—Quinine, 15 grains, t.d.s.; rectal quinine, 20 grains, in saline, 10 ounces.

---

4/1/18—Temperature 97° F.; pulse 80; respirations 20; urine in twenty-four hours = 41 ounces; improvement maintained.

*Treatment.*—Quinine, 15 grains, t.d.s.; rectal quinine, 20 grains, in saline 10 ounces.

---

5/1/18—Urine in twenty-four hours = 49 ounces; appetite better.

*Treatment.*—Quinine sulph., 15 grains, t.d.s., to be continued daily.

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6/1/18—Patient says he feels much better than he has done since the beginning of his illness. Urine in twenty-four hours = 50½ ounces; colour dark straw; urate deposit not so heavy.

13/1/18—Up to-day. Takes ordinary diet well. Urine quite clear; specific gravity 1012; acid; no albumin.

16/1/18—Out of doors to-day; quite recovered.

1/2/18—Photographed assisting the Medical Officer to give an intramuscular of quinine to another blackwater fever patient.

10/2/18—Still waiting for transport to England. Continuing quinine, 15 grains, t.d.s., and doing well on it.

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*Comments.*—It was very fortunate that Sir Ronald Ross happened to be visiting the hospital, and saw this case in the acute stage, because it assisted me in arriving at an

estimate of the advantage of using quinine in cases of blackwater fever.

It is necessary to explain that although Sir Ronald Ross gave a bad prognosis when he saw the urine, he told me later that as there was no sign of suppression he would alter his opinion, and said he thought that the patient would recover if he was treated with sod. bicarb., 15 grains every hour, and not given any quinine—in accordance with Koch's view on the subject.

As will be seen, I took this advice and refrained from using any quinine for eighteen hours. The next morning (December 23, 1917), finding the jaundice more marked, frequent vomiting, the urine if anything darker in colour, and malignant tertian parasites in the blood, I ordered 80 grains of quinine to be given within the next twelve hours.

The result was that the urine cleared up, but the patient was found to be quite blind eight hours after the full amount of quinine had been injected. There was complete loss of vision for four hours, and then the sight gradually returned and was nearly normal when the consulting ophthalmologist saw the patient six hours later; this result was obtained by stopping the quinine and substituting rectal salines, and strychnine subcutaneously. No quinine was given for two and a-half days until a rise of temperature occurred (on December 26, 1917), when it was necessary to give an intramuscular of 20 grains.

After this, 15 grains of quinine t.d.s. by the mouth daily, with an occasional intramuscular injection was tried, until December 31, 1917, but proved insufficient to prevent a relapse, and an intravenous had to be given on that date as well. The next day (January 1, 1918) patient again received 85 grains (including oral quinine). This, followed by 65 grains a day for three days, and then

15 grains t.d.s. by mouth for over a month sufficed to cure the blackwater fever and prevent a relapse of the malaria. Moreover, his eyesight caused no further anxiety although he had received over 2,000 grains of quinine in six weeks—an average of 47 grains a day.

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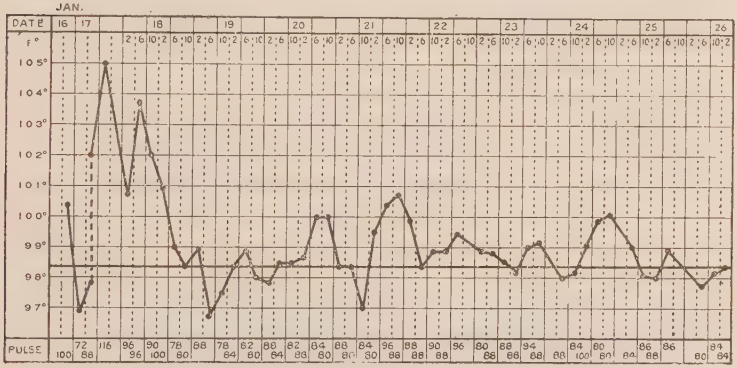
CASE 2. *Recovery from Blackwater Fever.*—Private E., aged 27. Service, 2 years 2 months. Admitted January 16, 1918. In Balkans, 1 year 7 months. Malaria January, 1916, and six times since.

*Onset of present illness:*—To-day, January 16, 1918.

*Symptoms.*—Headache, pains in back and limbs, shivering, sweating and vomiting.




Case 2. Private E.

*On admission.*—Temperature 100·5° F., falling; perspiring freely; tongue clean and moist; pulse 100, regular; heart impure mitral, first sound occasionally reduplicated; no dilatation; spleen plus and tender.

*Treatment.*—Calomel, 5 grains, and mag. sulph., quin. sulph., 15 grains t.d.s.

---

17/1/18—Much better. Temperature 97° F.; pulse 72.

8 p.m. Rigor. Temperature 105° F.

*Treatment.*—Mist. diaphoretic. Intramuscular quinine, 20 grains. Quinine sulph., 15 grains, t.d.s.

18/1/18—3 a.m. Temperature 100·4° F.; pulse 96.

6 a.m. Temperature 103·6° F. Passed porter-coloured urine. Icteric tinge of skin.

*Blood film :* No parasites found.

Urine : Fair amount of albumin.

Laboratory Report: "Large amount of granular deposit; very scanty epithelial cells; very occasional red cells."

2 p.m. Temperature 100·8° F.; pulse 100. Patient has vomited a few times and sweated freely.

5 p.m. Colour of urine slightly less dark; appears to be passing a normal quantity.

6 p.m. Temperature 99° F.; pulse 78; vomiting.

*Treatment.*—

10 a.m. Intravenous quinine, 30 grains.

11 a.m. Intramuscular quinine, 20 grains.

19/1/18—Patient states that for a short time during the early morning he was unable to see anything, but when examined later on his eyesight had apparently returned to normal. Urine in twenty-four hours — 6 a.m. to 6 a.m. = 40 ounces. Colour of urine a little less deep.

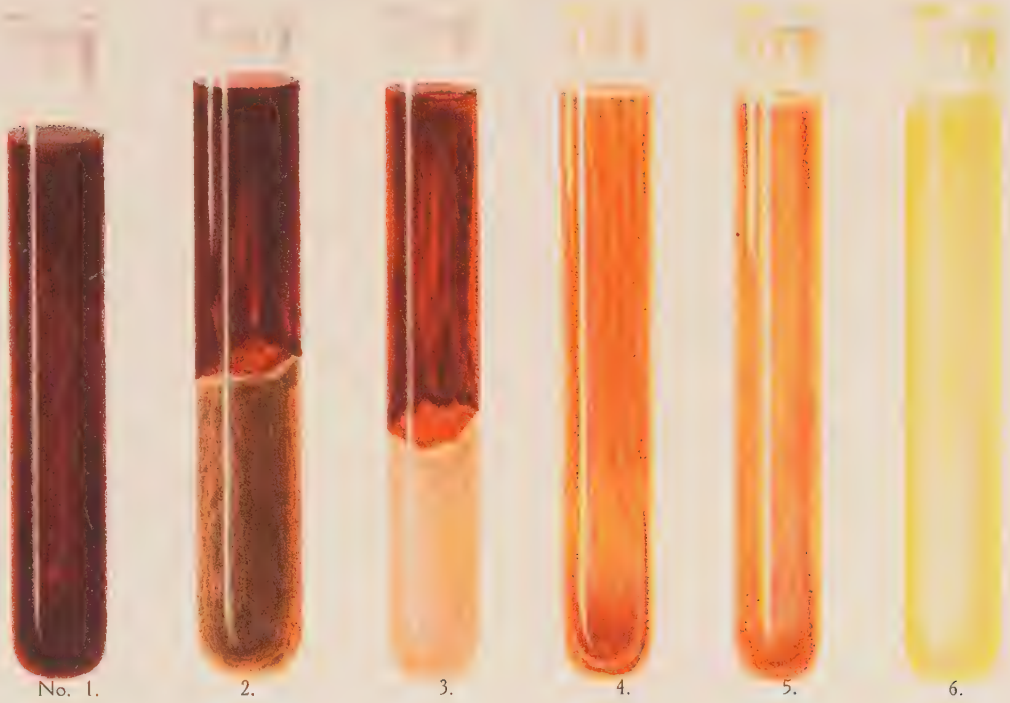
6 p.m. Patient vomited at times during the day—otherwise comfortable.

9 p.m. Temperature 98° F.; pulse 80.

11 p.m. Passed urine of an amber colour apparently free from hæmoglobin.

Laboratory Report on successive specimens of urine passed last night and this morning : " Three urines show granular deposit (red cell debris), granular casts and large epithelial cells from bladder. The last specimen shows very much less deposit."

## Specimens of Urine in Blackwater Fever.




No. 1. Freshly passed urine in acute stage.

,, 2. Same urine after standing—showing copious deposit of debris.

No. 3. Next specimen—beginning to clear up.

Nos. 4, 5 & 6. Show gradual return to normal.

*See p.* 180.

*Treatment.*—Rectal saline and brandy during the night.

11 a.m. Intravenous quinine, 20 grains, in saline, 8 ounces; intramuscular quinine, 20 grains.

6 p.m. Quinine, 20 grains, per rectum, only retained three-quarters of an hour, so intramuscular quinine, 20 grains, given.

---

20/1/18—2 a.m. Urine clearer and of a pale straw colour. Urine in twenty-four hours = 53 ounces.

10 a.m. Temperature 98·6° F.; pulse 82. Icteric tinge of skin much less marked. Vomiting less frequent.

6 p.m. Temperature 98·8° F.; pulse 88. Urine passed during the day is free from hæmoglobin.

*Treatment.*—

3 a.m. Rectal saline with brandy.

10 a.m. Intramuscular quinine, 20 grains.

6 p.m. Intramuscular quinine, 20 grains.

21/1/18—Urine in twenty-four hours = 39 ounces.

---

Laboratory Reports: Urine of January 19 and 20: "All specimens show granular deposit (debris of red cells, &c.), epithelial cells from various parts of urinary tract. Casts (granular).

"First specimen shows: Large amount of granular deposit. Epithelial cells from bladder and kidney. Granular casts.

"Second and third specimens show: Much less granular deposit. Several cells from second layer of kidney, some tailed cells and some from bladder.

"Fourth specimen: Similar but rather less epithelium.

"Fifth specimen shows: Marked diminution of granular

deposit. All varieties of epithelial cells seen. Granular casts much more marked. Numerous crystals of phosphates and scanty oxalates."

Patient better; temperature normal; pulse 84; vomiting much less frequent and only of stomach contents, not bile.

6 p.m. Temperature 100·4° F.; pulse 96.

*Treatment.*—Quinine, 20 grains, per rectum.

Intramuscular quinine, 20 grains.

22/1/18—Urine in twenty-four hours = 48 ounces.

Laboratory Report on Urine of January 21, 1918: "Early specimens still show granular deposit epithelial cells, casts, but the last one has very little deposit at all. The colour is now practically normal."

Patient much improved. Temperature 98·8° F.; pulse 90. Taking more nourishment, only very occasional vomiting.

6 p.m. Temperature 99·2° F.; pulse 96. Tongue moist and clean.

*Treatment.*—

11 a.m. Quinine, 30 grains, in saline, per rectum.

6 p.m. Quinine bihyd., 10 grains, by mouth.

10 p.m. Quinine bihyd., 20 grains, by mouth.

---

23/1/18—Urine in twenty-four hours = 44 ounces. Temperature normal; pulse 88; no vomiting; tongue clean and moist.

*Treatment.*—Quinine bihyd., 15 grains t.d.s., continued daily.

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24/1/18—Urine in twenty-four hours = 44 ounces.

6 p.m. Temperature 100° F.; pulse 90. Patient quite comfortable, taking nourishment and quinine by mouth well; no sickness; colour of skin improving.

25/1/18—Urine in twenty-four hours = 40 ounces. Temperature normal; steady improvement.

31/1/18—Patient rather anæmic-looking.

*Blood Examination:* Hæmoglobin, 42 per cent.; red blood corpuscles, 1,856,000 per c.mm.; colour index, 1·13.

*Treatment.*—Quinine, 15 grains, t.d.s., still continued. Mist. arsenic tonic t.d.s. (in graduated doses).

---

14/3/18—Very marked improvement.

---

*Comments.*—(1) Note the history of malaria and the number of relapses.

(2) No parasites were found in the blood.

(3) The urine cleared up on early and vigorous treatment with quinine (intravenous, 30 grains, and intramuscular, 40 grains, in ten hours).

(4) It is interesting to observe:—

(*a*) The change of colour from a dark porter through various shades of red to the amber of normal urine.

(*b*) The granular debris (broken-down red blood corpuscles) of the earlier specimens giving place to epithelial cells and granular casts as the condition advanced, and finally the disappearance of the deposit altogether as the patient became convalescent.

(5) The transient amblyopia should also be noted.

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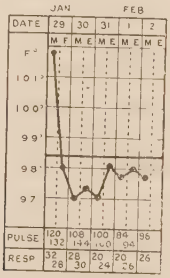
Case 3. *Death from Neglected Malaria* (*Blackwater Fever*).—Private G., aged 40. Service, 2 years 8 months. Admitted January 29, 1918. In Balkans, 1 year 2 months.

Previous history: Twice in hospital with malaria and many other slighter attacks. Says he has been ill with malaria almost continuously for the past five months.

Quinine taken by patient before admission. Says he has had two tablets every night since leaving the convalescent camp in November last, increased to four or six tablets every week or ten days, when he had one of his slight relapses.




Case 3. Private G.

Onset of present illness three days ago. Shivering, slight headache, pains in back and cramps in legs, vomiting. Says he noticed blood in his urine on day of admission.

---

29/1/18—12.45 p.m. *On admission.*—Icteric tinge of skin and conjunctivæ; temperature 101·8° F.; pulse 120, weak; heart sounds weak, no dilatation; spleen enlarged, firm; liver, no enlargement of liver dulness.

*Blood film:* Mononuclear excess; parasites not found.

2 p.m. Patient passed 8 ounces of dark red urine (blood colour) apparently containing large quantity of blood or hæmoglobin.

3 p.m. More urine passed, same colour. Pulse 136, weak.

Laboratory Report on Urine: "Granular debris (red cells and hæmoglobin). No other deposit."

4 p.m. Patient perspired freely after intravenous injection. Vomited a few times. Champagne, strychnine $\frac{1}{60}$ grain, digitaline $\frac{1}{100}$ grain 4-hourly. Rectal saline, 10 ounces, with brandy.

6 p.m. Temperature 98° F., pulse 132. Rectal saline, 10 ounces, with brandy.

7 p.m. Quantity of urine passed in the last six hours = 22 ounces.

10 p.m. Patient improved, not vomiting ; taking champagne and fluids well.

*Treatment.*—

2 p.m. Intramuscular quinine, 20 grains.

3 p.m. Intravenous quinine, 20 grains.

10 p.m. Intramuscular quinine, 20 grains.

---

30/1/18—9 a.m. Total quantity of urine, 7 p.m. to 7 a.m. = 34 ounces. Temperature 98° F. ; pulse 120, very feeble. Patient very collapsed during afternoon ; pulse not countable at wrist.

5 p.m. Temperature 98° F. ; pulse 144. Urine, 7 a.m. to 7 p.m. = 24 ounces.

Laboratory Report : "Large epithelial cells and casts are now present in addition to granular debris."

10 p.m. Urine now amber coloured ; no hæmoglobin.

*Treatment.*—

2 a.m. Rectal saline, 12 ounces, with brandy.

10 a.m. Intravenous quinine, 20 grains, strychnine, $\frac{1}{30}$ grains.

2 p.m. Rectal saline, 10 ounces, continued two-hourly.

11 p.m. Strychnine, $\frac{1}{60}$ grain, and digitalin, $\frac{1}{100}$ grain, four-hourly.

31/1/18—a.m. Patient improved this morning. Temperature 97° F.; pulse 100. No vomiting during the night. Has taken fluids freely but has only passed 6 ounces of urine from 7 p.m. to 7 a.m., urine quite clear.

---

Laboratory Reports on Urines passed on January 30, 1918: "Granular debris still in large amounts; epithelial cells still increased in number, a large proportion being from bladder. Epithelial and granular casts present."

p.m. Urine, 7 a.m. to 7 p.m. = 7 ounces. Patient has perspired freely.

*Treatment.*—

11 a.m. Intramuscular quinine, 20 grains.

---

31/1/18—℞ Pot. citrate.
Liq. ammon. acet.
Sp. æth. nitrosi.
Given hourly.
Hot fomentations to loins Blanket baths, &c.
Rectal salines four-hourly.

7 p.m. Liq. adrenalin 10 minims three-hourly.

---

1/2/18—Temperature 97·6° F.; pulse 84. Patient's general condition has been good all night and he has taken fluids well. Urine, 7 p.m. to 7 a.m. = 4¼ ounces.

Afternoon. Patient perspired freely.

Evening. Temperature 98° F.; pulse 95. Urine, 7 a.m. to 7 p.m. = 4¼ ounces.

Laboratory Reports on Urines of January 31, 1918: "Specimen 1: Less granular desposit, few casts, few cells (epithelial).

"Specimen 2: Large number of granular casts; large number of epithelial cells from superficial layer of kidney and from bladder."

*Treatment.* Rectal salines, 10 ounces, continued four-hourly day and night.

10 a.m. Quinine, 15 grains, by mouth.

3 p.m. Intramuscular quinine, 20 grains.

5.30 p.m. Hot pack.

7 p.m. Sp. ætheris nitrosi, 1 drachm, repeated hourly for four hours to maintain perspiration.

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2/2/18—Temperature 97·6° F.; pulse 96. Has perspired freely all night. Has taken fluids well and retained salines. Urine, 7 p.m. to 7 a.m. = 3 ounces. Urine appears to be quite clear and contains only a moderate amount of albumin.

Laboratory Report on Urines passed on February 1, 1918: (1) "Specimens still show granular deposit but in decreased amounts. Epithelial cells from kidney, tailed and superficial. Also from bladder. Granular casts."

(2) At 5 a.m. on February 2, 1918: "Very little deposit, few epithelial cells." Patient perspiring freely.

2 p.m. Slight twitchings of muscles of face.

2-5 p.m. Died suddenly. Urine 7 a.m. to 2 p.m. = 2 ounces only.

*Treatment.*—

10 a.m. Quinine, 15 grains, by mouth; rectal salines 4-hourly.

11.50 a.m. Hot pack.

---

*Post-mortem Report.* — Brain: Marked pallor, no petechiæ present.

Lungs: Congestion at both bases; left apex tuberculous.

Heart : Much dilated; muscle pale, atrophic and fatty in appearance; soft and doughy to touch. Walls of left ventricle did not exceed ½ inch in thickness. Moderate degree of senile atheroma of aorta.

Liver : Enlarged, fatty and bile-stained.

Spleen : Three times normal size, dark, soft, and diffluent. Slight perisplenitis.

Kidneys : Slightly enlarged and very pale; no congestion apparent; capsule strips readily.

Supra-renals : Pale. All organs were anæmic.

*Report on Sections of Tissue sent to Base Laboratory.*—

Liver : Necrosis in centre of lobules and considerable degeneration. Melanin present.

Brain : Normal. No parasites seen.

Supra-renals : Considerable degeneration of cortex and medullary cells.

Spleen : Melanin present—plus, plus.

Kidney : Marked tubular degeneration affecting convoluted tubules; tubules contain debris and blood casts.

Because the case was an extremely interesting and important one, we wrote to the Base Laboratory for the sections and on examination found :—

Liver : Chronic venous congestion. Central veins and capillaries of lobule distended. Deposition of blood pigment excessive and generalized, but mostly grouped round the centre of the lobule. Necrosis of liver cells in centre of lobule and cloudy swelling for some distance from the centre. The changes appeared to be due to chronic venous congestion and to the deposition of malarial pigment.

Kidney : Marked cloudy swelling and necrosis of *epithelium of convoluted tubules;* convoluted tubules distended and filled with debris and blood casts. No

glomerular or interstitial changes. Intertubular vessels empty. Larger veins congested.

The changes appeared to be a secondary condition, due to the action of the toxins upon the cells of the convoluted tubules. There was no evidence of primary acute nephritis.

*Note.*—The epithelial cells of convoluted tubules showed a loss of nuclear staining but in some cases the nuclei were apparently normal. It was impossible to estimate the percentage of damaged cells.

*Comments.*—(1) Patient was 40 years old and looked much older than his stated age.

(2) He had a history of almost continuous malarial attacks treated with quinine tabloids, 10 grains a day. It is quite certain that he absorbed very little and that it had no effect in stopping the relapses or preventing a fulminating and fatal attack of blackwater fever.

(3) This history of chronic malaria insufficiently treated with quinine is the main feature of every case of blackwater fever that has come under my charge.

(4) It will be seen that the patient was given quinine 60 grains intravenously and intramuscularly on the day of admission and about 20 grains daily afterwards. The reason for reducing the amount of quinine was the bacteriological report which stated that there were red cells in the early specimens of urine. I considered that this might be a case of nephritis and not a true blackwater fever, and cut down the quinine accordingly. I have since found that there were very scanty red cells and the post-mortem section shows that there was no primary acute nephritis.

The urine cleared up after the injection of quinine on the first day but the total quantity passed during each succeeding period of twelve hours gradually became less and less until total suppression supervened.

The patient was quite conscious until his death, which was very sudden. Slight twitchings of the muscles of the face were the only premonitory signs.

I do not think any treatment could have saved this man because of his extremely toxic condition, the advanced degenerative changes in his spleen and other organs and the enormous damage to the epithelium of the convoluted tubules of his kidneys. Quinine will cure the vast majority of cases of blackwater fever, but in a small percentage it fails. The latter are the very severe cases with a history of long-standing malaria which has been insufficiently treated. Quinine, administered immediately hæmoglobin appears in the urine, clears it up very quickly, but in the late stages when much destruction of urinary epithelium has taken place no treatment appears to be able to prevent suppression and death.

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CASE 4. *Blackwater Fever.*—Private H., aged 20.

*Notes from — General Hospital :—*

18/1/18—Four admissions to hospital with malaria. Onset, two days ago. Headache, shivering, &c.; temperature 101·8° F.; spleen palpable.

24/1/18—Temperature settled; patient very anæmic; some giddiness.

*History of Quinine Dosage at — General Hospital :—*

From January 18, 1918, 45 grains daily for three days; 30 grains daily for five days; 15 grains daily for eight days.

5/2/18—Admitted 28th General Hospital. Temperature 98·4° F.; pulse 96; headache and giddiness; heart and lungs normal.

*Treatment.*—Quinine, 15 grains, t.d.s.

6/2/18—Skin sallow and slightly jaundiced; conjunctivæ, icteric tinge; spleen enlarged, not tender; liver, no enlargement; passed urine of dark port wine colour.

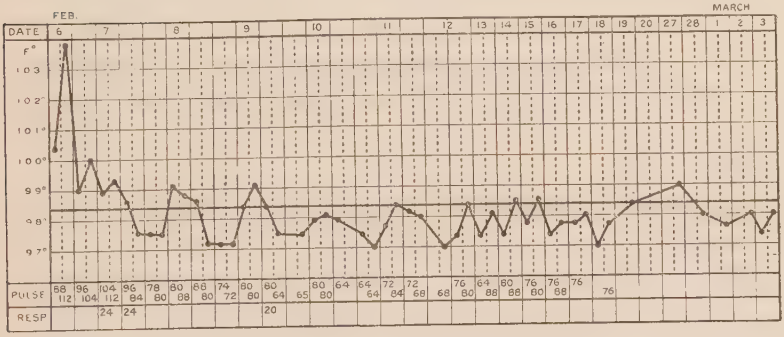
*Blood film :* No parasites found.

12.30 p.m. Urine slightly less dark in colour.

3 p.m. Urine passed is decidedly lighter.

6 p.m. Temperature 100·4° F. ; pulse 88.

6.30 p.m. Urine much improved ; shows only a small amount of hæmoglobin ; total quantity in nine hours = 33 ounces.




Case 4. Private H.

7.45 p.m. Colour darker again.

9 p.m. Almost a port wine colour.

Patient then had a rigor and at 10 p.m. his temperature was 103·8° F. ; pulse 112 and good.

Laboratory report on urine passed at — 11 a.m. : "Hæmoglobin, granular deposit (debris of red cells), scanty red cells, very scanty epithelial cells. 6.30 p.m. : Very little deposit. 7.45 p.m. : Granular debris with occasional epithelial cells. 9 p.m. : Granular debris, very scanty red cells, renal epithelial cells."

*Treatment.—*

11 a.m. Rectal saline, 20 grains.

6 p.m. Quinine bihyd., 20 grains, by mouth.

9 p.m. Intramuscular quinine, 20 grains.

7/2/18—Urine in twelve hours, 7 p.m. to 7 a.m. = 40 ounces. Specimens passed at 4.30 and 6.40 a.m. were of a dark port wine colour with much sediment. Temperature 99° F.; pulse 104; tongue furred and moist. Patient vomited twice after intravenous quinine injection but was able to take fluid nourishment later on.

Urine at 1.30 p.m. lighter in colour; at 5.30 p.m. still lighter (orange colour).

6 p.m. Temperature normal; pulse 84 per minute. Urine in twelve hours, 7 a.m. to 7 p.m. = 21 ounces.

Laboratory report on urine passed at—4.30 a.m.: "Similar to last specimen (that of 9 p.m. on February 6, 1918), but more marked granular casts. 1.30 p.m.: Scanty granular deposit with epithelial cells from bladder, &c. —a marked improvement."

*Treatment.*—

10 a.m. Intravenous quinine, 30 grains, in saline, 8 ounces.

2 p.m. Rectal saline with quinine, 20 grains.

5 p.m. Rectal saline with quinine, 20 grains.

10 p.m. Intramuscular quinine, 20 grains.

8/2/18—Successive specimens of urine show constant improvement. The one passed at 6 a.m. shows much deposit of urates but is apparently free from hæmoglobin, and that passed at 9 a.m. is quite clear.

Patient is much better. Had two plain rectal salines (10 ounces) during the night, took fluids well and has not vomited.

10 a.m. Temperature 99° F.; pulse 80 per minute. Quantity of urine in twelve hours, 7 p.m. to 7 a.m. = 21½ ounces.

Laboratory report on specimen passed at—9 a.m.: "Small amount of granular deposit, rather larger number of epithelial cells, bladder; some casts. 10.30 a.m.: Deposit much less in quantity; few cells present."

*Treatment.*—

10 a.m. Rectal saline with quinine, 20 grains.

2 p.m. Intramuscular quinine, 20 grains.

6 p.m. Rectal saline with quinine, 20 grains.

Evening. Continued improvement. Temperature 98·6° F.; pulse 88. Urine in twelve hours, 7 a.m. to 7 p.m. = 35 ounces.

9/2/18.—Temperature 97·4° F.; pulse 76. Patient much improved; tongue clean and moist. Urine in twelve hours, 7 p.m. to 7 a.m. = 26 ounces.

6 p.m. Temperature 98·4° F.; pulse 80. Urine still contains a little albumin.

Laboratory report on specimens passed at: 6.30 a.m. and 5.25 p.m.—"Epithelial cells very scanty; small amount of granular debris still present."

*Treatment.* Quinine bihyd. 15 grains, by mouth four times.

10/2/18.—Temperature and pulse normal. Patient doing very well. Urine, no albumin present. Quantity in twelve hours, 7 p.m. to 7 a.m. = 29 ounces.

6 p.m. Temperature 97·8° F.; pulse 64. Urine in twelve hours, 7 a.m. to 7 p.m. = 38¼ ounces.

*Treatment.*—Quinine, 15 grains t.d.s. Rectal saline with quinine, 15 grains.

11/2/18—Temperature, 97.6° F.; pulse 72. Urine, 7 p.m. to 7 a.m. = 29¼ ounces.

7 p.m. Continued improvement. Urine, 7 a.m. to 7 p.m. = 49¼ ounces.

*Treatment.*—Quinine, 15 grains, t.d.s. to be continued daily.

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12/2/18—Temperature and pulse normal. Urine in twenty-four hours = 53 ounces.

13/2/18—Urine in twenty-four hours = 57 ounces.

14/2/18—Urine in twenty-four hours = 63 ounces.

18/2/18—Steady and satisfactory progress. No further rise of temperature and no signs of recurrence of urinary symptoms.

7/3/18—Continued improvement. No relapse; accounted for by his having had quinine, 15 grains, t.d.s., daily.

*Blood Count.*—Hæmoglobin, 72 per cent.; red blood corpuscles, 3,570,000 per c.mm.; colour index, 1.

*Comparison with Case* 3 (Pte. G.).

| Pte. G. (Case 3). | Pte. H. (Case 4). |
|---|---|
| Admitted January 1, 1918. Three times in hospital and many slight attacks of malaria. Jaundiced and passed dark red urine. | Admitted February 5, 1918. Four admissions to hospital with malaria. Jaundiced, and passed port-wine coloured urine. |
| *Blood film:* Mononuclear increase; no parasites found. | *Blood film:* No parasites found. |
| *Progress and Treatment.*—Received quinine 60 grains in eight hours—one intravenous and two intramuscular—on January 29, | *Progress and Treatment.*—Patient received 40 grains of quinine in seven hours (11 a.m. to 6 p.m. on February 6, 1918). Urine |

1918. Urine cleared up within the next twenty-four hours, quantity passed in this period 58 ounces. Quinine reduced to 20 grains daily on January 30, 1918. On the following day signs of suppression became evident—13 ounces in twenty-four hours. Urine remained clear, and quinine treatment was not altered (20 grains per diem). The urine in the next twenty-four hours only amounted to 8½ ounces. Quinine 15 grains, by mouth, was then given in addition to the daily intramuscular of 20 grains, but the amount of urine still diminished—5 ounces only being passed in the nineteen hours immediately before his death.

*Result.*—Total suppression of urine and death in four days.

became lighter; but at 7 p.m. got darker again and was port-wine coloured at 9 p.m. He then had a rigor. In the next twenty-five hours (from 9 p.m. on February 6, to 10 p.m. on February 7, 1918) patient received 110 grains of quinine intravenously, intramusculary and *per rectum;* and during this time he passed 61 ounces of urine. Twelve hours later, at 9 a.m., on February 8, 1918, the urine was quite clear and he was much improved. He received quinine 60 grains on February 8, and passed 56½ ounces of urine in the twenty-four hours. For the next three days he received 60 grains a day, and passed a normal amount of urine each day.

*Result*—Complete recovery.

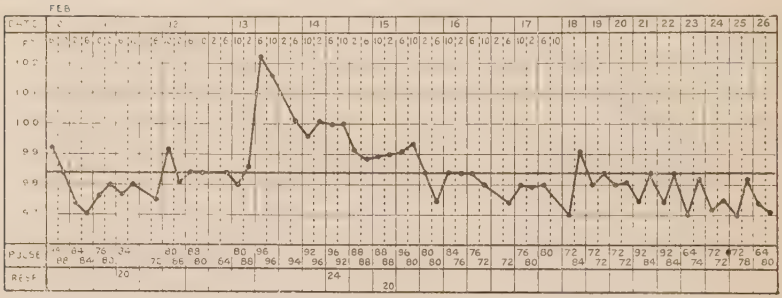
*Comments.*—(1) Here again the change from a dark to a light colour and its relation to the amount of debris, epithelial cells and casts in the urine should be noted.

(2) If some "unknown agent" and not malaria is the cause of blackwater fever then, it appears to me, quinine

is of extraordinary value in combating the effects of "unknown agents."

(3) If blackwater fever is due to quinine then the reason for the recovery of Private H. who received 110 grains in the twenty-five hours immediately following his relapse is inexplicable.

CASE 5. *Blackwater Fever.*—Private W., aged 40. Service, 1 year 8 months. Admitted on February 10, 1918. In Balkans, twelve months.




Case 5. Private W.

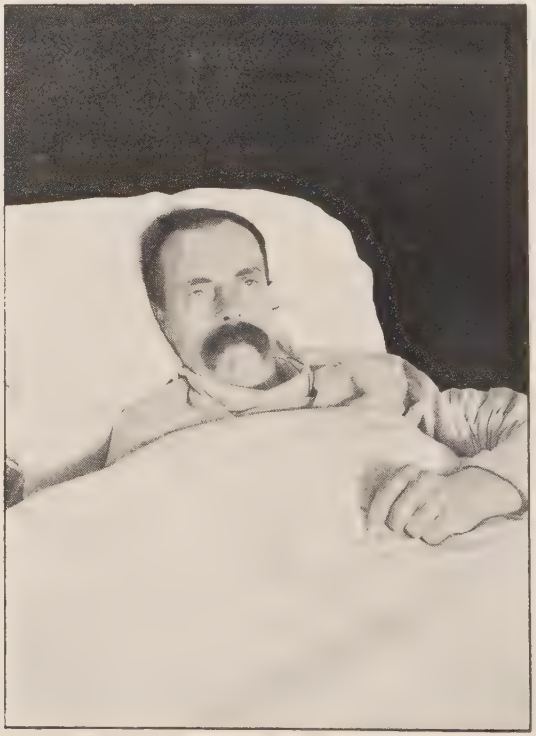
In hospital with malaria in July, 1917. Many relapses. Patient treated his relapses with occasional doses of quinine.

*Onset of present illness:*—Four days ago. Shivering, headache, giddiness. For the last two days patient says he has passed very little urine. Anorexia and pain in epigastrium.

*On admission.*—Temperature, 99·4° F.; pulse 80, good; jaundice slight; tongue moist and furred; no vomiting; spleen enlarged and tender (1½ inches below costal margin); liver not enlarged; urine, muddy port-wine colour.

*Blood film:* Benign tertian gametocytes.

CASE 4.—Private H. Taken during the acute stage of an attack of blackwater fever. (See p. 204.)



CASE 5.—Private W. Taken during the acute stage of blackwater fever.

Urine passed at 11 p.m. showed much less hæmoglobin; and that passed at 1.15 a.m. apparently contained none.

*Treatment.*—

7.30 p.m. Rectal saline with quinine 20 grains.
8.30 p.m. Intramuscular quinine 20 grains.
11 p.m. Intramuscular quinine 20 grains.

Laboratory Report on Urine passed at 7 p.m. (February 10, 1918): "A certain amount of granular debris; many degenerated epithelial cells; granular and epithelial casts." 11 p.m. (February 10, 1918): "Less granular deposit; more non-degenerate epithelial cells." 1.15 a.m. (February 11, 1918): "Very little granular deposit; *very scanty* red cells; epithelial cells from all parts; casts." 6 a.m. (February 11, 1918): "Similar, but less of everything; no casts." Urine passed in twelve hours, 7 p.m. to 7 a.m. = 21½ ounces.

11/2/18—Patient improved. Temperature, 98·6° F.; pulse 76. Urine passed at 6 a.m. (see above) quite clear.

6 p.m. Temperature, 97·8° F.; pulse 84. Urine passed in twelve hours, 7 a.m. to 7 p.m. = 43¼ ounces.

Laboratory Report on Urine passed at 9.45 a.m.. "Free granular deposit very scanty; very numerous epithelial cells which contain granular deposit."

Patient has taken fluids well; no vomiting.

*Treatment.*—

10 a.m. Rectal saline with quinine, 20 grains.
2 p.m. Intramuscular quinine, 20 grains.
6 p.m. Rectal saline with quinine, 20 grains.

---

12/2/18—Patient much better. Temperature, 99·2° F.; pulse 80. Tongue much cleaner and moist; urine remains free from hæmoglobin, occa-

sionally cloudy with urates and contains a very little albumen. Urine passed in twelve hours, 7 p.m. to 7 a.m. = 31¾ ounces.

Laboratory Report on Urine passed at 11 a.m.: "Same as specimen passed at 9.45 a.m. on February 11, 1918. 6 p.m. Temperature and pulse normal."

*Treatment.*—Quinine sulph., 15 grains, t.d.s.

2 p.m. Intramuscular quinine, 20 grains.

---

13/2/18—Temperature, 98° F.; pulse 84. Improving. Tongue practically clean, and moist; urine in twelve hours, 7 p.m. to 7 a.m. = 18 ounces.

6 p.m. Temperature rose suddenly to 102·4° F.; pulse 96. Tongue moist but rather coated. Patient did not complain of shivering. No recurrence of blackwater. Urine in twelve hours, 7 a.m. to 7 p.m. = 16 ounces. Patient perspired freely after rectal injection.

*Treatment.*—Quinine, 15 grains, t.d.s.

6 p.m. Rectal saline with quinine, 20 grains.

14/2/18—Temperature, 99·6° F.; pulse 92. Tongue moist but furred. Urine in twelve hours, 7 p.m. to 7 a.m. = 17 ounces. No hæmoglobinuria, but thick deposit of urates.

---

*Second blood film* taken; negative.

6 p.m. Temperature 100° F.; pulse 96. Urine in twelve hours, 7 a.m. to 7 p.m. = 24 ounces.

*Treatment.*—

10 a.m. Intramuscular quinine, 20 grains.

4 p.m. Rectal saline with quinine, 20 grains, also quinine, 15 grains, t.d.s.

---

15/2/18—Patient improved. Tongue slightly furred but moist. Temperature, 99° F.; pulse 88.

After recovery from blackwater fever.
Left to right—Case 2, Private E. ; Case 4, Private H. ;
Case 5, Private W.

Face p. 212.

Evening. Temperature, 99·2° F. Urine in twenty-four hours = 74 ounces.

*Treatment.*—Quinine, 15 grains by mouth, given four times during the day.

---

16/2/18—Temperature normal; pulse 80. Urine in twenty-four hours = 55 ounces.

*Treatment.*—Quinine, 15 grains, t.d.s., to be continued daily.

---

17/2/18—Continued improvement. Temperature, 98° F.; pulse 76. Urine in twenty-four hours = 61 ounces.

18/2/18—Slight rise of temperature in evening, 99·2° F.

*Treatment.*—An extra dose of quinine, 15 grains given. Urine is now free from albumin. Amount in twenty-four hours = 54 ounces.

---

20/2/18—Temperature keeping normal.

2/3/18—Continued improvement. Patient up for one hour to-day.

7/3/18—No relapse since 18th ultimo. Quinine, 15 grains, t.d.s., still continued.

*Comments.*—On account of his age and the severity of the attack this man caused us considerable anxiety. Fortunately, when he was admitted, the destruction to the urinary epithelium of his kidneys was not so far advanced as to prevent recovery under proper quinine treatment.

CASE 6.—*Blackwater Fever* with quinine amblyopia. Corporal M., aged 27 years. Admitted February 25, 1918. In Balkans, 1 year 2 months.

*Previous History.*—First admitted to this hospital on *October* 27, 1917, suffering from *malaria*. He had been in hospital with malaria twice before.

*On first admission* (*October* 27, 1917):—

*Symptoms.*—Headache, shivering, vomiting, diarrhœa and abdominal pains. Temperature, 104° F.; pulse 136. Very anæmic; skin, icteric tinge; tongue, moist, brown fur; eyes, icteric and injected; lips, herpes; spleen, much enlarged (reaching to umbilicus), firm and tender; abdominal tenderness.

*Blood film:* Malignant tertian crescents.

*Treatment.*—Patient was given quinine, 15 grains, t.d.s., for a fortnight, and then 30 grains daily for about five weeks. He received 1,755 grains in fifty-one days. Daily average = 34 grains.

---

He had no relapse during this time and improved to such an extent that although he had passed a Hospital Ship Board in November, it was considered advisable to remove him from the list and send him back to his unit, to await an opportunity of returning to England by ordinary transport. He left the hospital on December 17, 1917, feeling quite fit, but still had a rather tender spleen.

I asked each of the ex-hospital ship patients to write and let me know if they relapsed, and strongly advised them to take at least 30 grains of quinine a day.

From Corporal M.'s own statement it appears that he was so disgusted at having been taken off the hospital ship list after waiting so long to go home, that he resolved that whatever happened he would not again report sick and return to hospital.

After his discharge to the convalescent depot and subsequent return to his unit, he received about 685 grains in forty-five days, made up as follows:—

Quinine, 45 grains daily for three days (during a relapse); 15 grains daily for two weeks; 10 grains daily

for two weeks ; 15 grains daily for two weeks. Average quinine = 15 grains daily.

He states that notwithstanding this treatment he relapsed frequently, but did not report sick until he developed *blackwater fever,* when he was sent to hospital by the Regimental Medical Officer. I saw him immediately after admission, and found his condition to be so grave that it was impossible to hold out any hope at all of his recovery.

The detailed notes of the case are as follows :—

*History immediately before re-admission :—*

20/2/18—Severe rigor.

22/2/18—Another relapse.

24/2/18—Rigor, vomiting, sweating ; patient passed "blackwater" in the evening.

25/2/18—*Re-admission to 28th General Hospital :* Very marked jaundice of skin and conjunctivæ ; tongue, moist, furred, greenish-yellow in colour ; temperature, 102° F. ; pulse 100 per minute, regular ; heart, muffled sounds, mitral systolic bruit ; spleen, enlarged, 1 inch below costal margin, very tender ; liver, slight enlargement, dulness just below costal margin, very tender, especially over gall bladder.

*Blood film :* Large increase of mononuclears ; scanty degenerate gametocytes (benign tertian).

Urine : Dark porter colour ; very intense "blackwater."

Laboratory Report : "Large amount of granular deposit ; several large epithelial cells ; granular casts."

Evening. Temperature, 105° F. ; pulse 112. No visible change in urine ; total quantity from noon to 7 p.m. = 15½ ounces.

10.30 p.m. Temperature, 103·6° F. ; pulse 108.

*Treatment.*—

12.15 p.m. Intramuscular quinine, 20 grains.

2.30 p.m. Intravenous quinine, 30 grains, in 8 ounces saline.

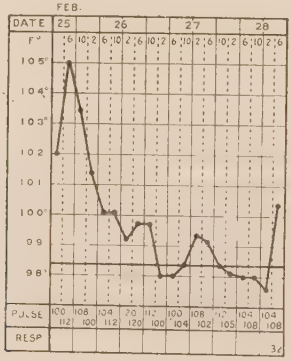
10.30 p.m. Intramuscular quinine, 20 grains.

2 a.m. Rectal saline with quinine, 20 grains.

---

26/2/18—Urine in twelve hours, 7 p.m. to 7 a.m. = 27½ ounces. Restless night; frequent vomiting: cannot even retain champagne.

6 a.m. Rectal saline.




Case 6. Corporal M.

9 a.m. Jaundice very marked still; no apparent change in urine; respirations 100·2; pulse 112.

2 p.m. Temperature, 99·4° F.; pulse 120 and weak.

7 p.m. Patient has hiccoughed occasionally. Urine in twelve hours, 7 a.m. to 7 p.m. = 29 ounces.

*Treatment.*—

11 a.m. Intravenous quinine, 30 grains, in 8 ounces of saline.

3 p.m. Strychnine, $\frac{1}{30}$ grain; digitaline, $\frac{1}{100}$ grain.

4 p.m. Rectal saline.
6.15 p.m. Subcutaneous saline, 14 ounces.
9.40 p.m. Intramuscular quinine, 20 grains.
10 p.m. Strychnine, $\frac{1}{60}$ grain, digitaline, $\frac{1}{100}$ grain, repeated 4-hourly.
11.30 p.m. Rectal quinine not retained.

---

27/2/18—Urine in twelve hours, 7 p.m. to 7 a.m. – 4 ounces; colour very dark.

9 a.m. Temperature normal; pulse 104, weak; colour of skin improved; less jaundice; bilious vomiting continues; urine this morning (3 ounces passed at 9 a.m.) is coffee-coloured with large amount of light brown sediment, three-quarters of a test-tube filled with precipitate.

*Amblyopia.*—In the early morning patient complained that he was unable to see anything, and on examination I found he was quite blind.

---

12.30 p.m. Consulting Ophthalmologist saw patient and made the following notes: "Both eyes—optic discs good colour; retinal vessels of normal size; pupils equal, no contraction to light; no perception of light in either eye." Quinine stopped.

1.55 p.m. Passed $1\frac{1}{8}$ ounce of urine containing large amount of sediment, but supernatant urine apparently not containing any hæmoglobin

Laboratory Reports on Urines passed at—12.30 p.m. February 26, 1918: "Very little granular deposit; scanty cells." 9.30 a.m., February 27, 1918: "Very large amount of granular deposit; numerous large urinary epithelial cells; granular casts."

Evening. Temperature, 99·2° F.; pulse 208. Total urine in twelve hours = $4\frac{1}{8}$ ounces.

*Treatment.*—Rectal salines 2-hourly. Strychnine and digitaline 4-hourly.

---

28/2/18—Rather drowsy during night; retained rectal salines; occasional vomiting; sight not yet improved. Urine in twelve hours (night) = $3\frac{1}{4}$ ounces passed at 1.45 a.m.

9 a.m. Temperature, 98° F.; pulse 108.

11 a.m. Sight returning; says he can see buttons and badges on tunic of Medical Officers.

11.5 a.m. Passed $2\frac{1}{2}$ ounces of urine; each successive urine is clearer and contains less deposit, but the amounts indicate partial suppression.

Sight improved, and he was able to distinguish faces during the afternoon. General condition became gradually worse; respirations more rapid.

Laboratory Report on Urines passed—February 27, 1918: "Cells (epithelial) increased in amount; granular deposit still abundant." February 28, 1918: "Deposit much less; cells and casts decreased."

3.45 p.m. Passed 2 ounces of urine.

6 p.m. Respirations rapid; occasional cough; temperature, 100·4° F.; pulse 108; patient vomited and seemed worse afterwards.

*Treatment.*—Rectal salines, and strychnine and digitaline.

9.50 p.m. Died suddenly.

*Post-mortem Notes.*—Brain: Anæmic.

Heart: Dilated—muscle soft and doughy to touch. Ventricle walls greatly thinned—muscle pale and yellowish. All the chambers dilated. Valves normal. Pericardium contains straw-coloured fluid.

Lungs: Congested.

Liver: Much enlarged, mottled with yellow fatty areas and areas showing venous congestion. Sub-peritoneal petechiæ on right diaphragmatic surface.

Spleen: About five times normal size, soft, but not quite diffluent; dark red colour. The spleen was more firm and not quite so black as that usually found in fatal acute malignant malaria.

Kidneys: Both enlarged and congested; firm and full to touch; capsule strips readily. No special features seen on naked-eye inspection of cut surface.

Suprarenals: No visible change.

Omentum: Showed scattered capillary hæmorrhages.

The other organs were normal.

*Comments.*—(1) The history of the case is very similar to that of Private G. (Case 3).

(2) The term "neglected malaria," describes the disease more accurately than the name "blackwater fever." The dark colour of the urine is merely a sign appearing late in the course of a disease in which we find constant malarial relapses, due to insufficient quinine treatment, progressive degeneration of the internal organs, excessive blood destruction, damage to epithelium of the convoluted tubules of the kidney, "black water," suppression of urine, sudden cardiac failure, and death.

(3) The death of this man is another nail in the coffin of the "small dose method" of treating malaria. If his misfortune should assist others to avoid the catastrophe which overtook him, then, at least, he will not have died in vain.

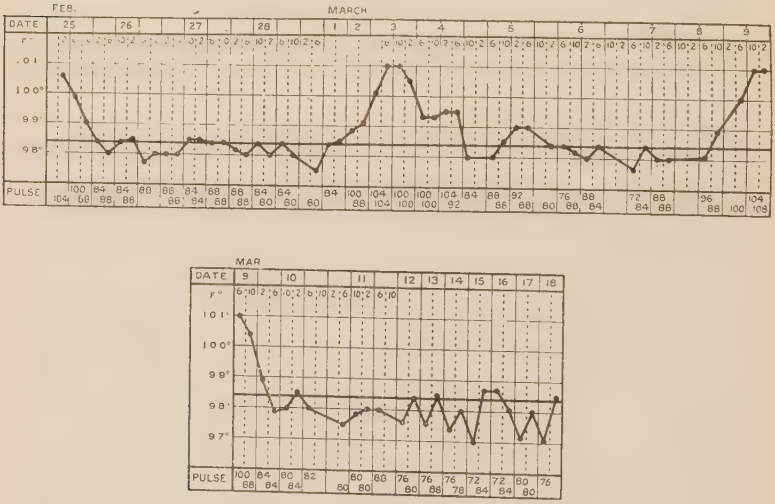
(4) The amblyopia, following on the administration of 70 grains of quinine a day on two successive days, goes to show that when the drug accumulates in the system—due to failure of the kidneys to excrete it sufficiently

rapidly—the effect produced on the sight is identical with that following the administration of a very large single dose.

(5) The post-mortem notes on the heart, spleen, liver and kidneys should be carefully studied.

*Notes.*—Further comments on the case will be found in the chapter on "The Treatment of Chronic Malaria" (p. 130).

CASE 7.—*Blackwater Fever* (with quinine amblyopia). Private B., aged 28. Service, 1 year 8 months. Admitted February 25, 1918. In Balkans, 1 year 1 month.




Case 7. Private B.

*History.*—Five times in hospital with malaria since August, 1917.

Quinine taken recently: Has had 30 grains a day for the last four days. Previous to this he had only occasional doses when feeling unwell.

*Onset:*—Four days ago. Shivering, headache, vomiting,

no sweating; passed "blood in urine" the day before admission.

*On admission* (12.15 p.m.) Conjunctivæ jaundiced; tongue moist and slightly furred; pulse, regular, soft; heart sounds weak and muffled, no murmurs heard; cardiac dulness not increased; spleen, enlarged and tender, 1½ to 2 inches below costal margin, fairly firm consistence; liver, no enlargement of normal dulness, some tenderness, especially about the area of the gall bladder.

*Blood film:* Parasites not found; slight mononuclear excess.

Urine, dark muddy port-wine colour, apparently containing a fair amount of hæmoglobin.

Laboratory Report: "Cells from various parts of urinary tract, including columnar cells. Most of them show granular degeneration, some granular deposit (small amount), casts."

6 p.m. Temperature, 99·8° F.; pulse 100. Perspiring. Bilious vomiting troublesome. Quantity of urine from noon to 7 p.m. = 8 ounces.

*Treatment.*—

12.30 p.m. Intramuscular quinine, 20 grains.

3.30 p.m. Intravenous quinine, 30 grains.

9.30 p.m. Rectal quinine, 20 grains, only retained for three-quarters of an hour.

11.30. p.m. Intramuscular quinine, 20 grains.

---

26/2/18—Temperature, 98·4° F.; pulse 88. Urine passed in twelve hours, 7 p.m. to 7 a.m., = 21½ ounces. Specimen passed at 8.45 a.m. appears to be free from hæmoglobin.

*Amblyopia.*—Patient complained of blindness early this morning, and says this came on suddenly. His sight appears to be rapidly improving.

11.30 a.m. Report by Hospital Ophthalmologist: "According to patient's statements, his sight was normal yesterday afternoon. At daylight this morning he was only able to distinguish large objects, such as his locker and the windows. When examined at 11.30 a.m. he was able to read the newspaper with either eye. Pupils semi-dilated, react to light but rapidly dilate again. Fundi seen with some difficulty owing to inability of patient to fix the eye. On examination, right disc and whole of fundus somewhat paler than normal. There does not appear to be any alteration in the size of the vessels but both arteries and veins appear rather paler than normal. Left disc does not appear pale. Rest of fundus as in right eye."

5.12 p.m. Patient seen by Consulting Ophthamologist to the Forces, who made the following notes: "Optic discs of normal colour and retinal arteries of normal size. Congenital crescent at lower edge of optic disc."

6 p.m. Temperature, 97·6° F.; pulse 88.
Vomiting still troublesome. Urine in twelve hours = 17½ ounces.

Laboratory Reports on Urines passed at—1.10 a.m., February 26, 1918: "Epithelial cells from urinary tract, some showing granular degeneration, epithelial and granular casts; some granular debris." 5.30 a.m.: "Similar but less in amount." 8.40 a.m.: "Very little granular deposit; many cells and casts." 11.30 p.m.: "Large number of epithelial cells, mostly from kidney,

many of them filled with granular debris; very little free granular deposit; granular casts."

*Treatment.*—

6 a.m. Rectal saline with brandy. No quinine given to-day until evening.

6.45 p.m. Rectal saline with quinine, 20 grains given but not retained.

10 p.m. Intramuscular quinine, 20 grains.

---

27/2/18—Temperature, 97·6° F.; pulse 88. Has vomited frequently during night, but seems rather better this morning. Urine in twelve-hours = 10½ ounces.

6 p.m. Temperature, 98·4°; pulse 88. No vomiting to-day; tongue clean and moist.

Laboratory Reports on Urines passed at 2 a.m., February 27, 1918: "Definite coarse granules of cell debris; large number of large epithelial cells from urinary tract; granular casts; epithelial cells still somewhat engorged with granular debris."

12 noon, 27/2/18—Much less granular deposit; very numerous cells; more granular appearance.

*Treatment.*—

2 a.m. Rectal saline and brandy.

6 p.m. Quinine bihyd., 20 grains, given by mouth, but patient vomited after one and three-quarter hours.

8 p.m. Rectal saline with quinine, 20 grains (retained for one hour).

---

28/2/18—Temperature, 98° F.; pulse 88. Patient much improved. Urine cloudy and contains a little albumin; amount in twelve hours = 13 ounces.

Laboratory Reports on urines passed at 4 a.m., February 28, 1918: "Very little debris and not so coarse; otherwise as in previous specimens."

6 p.m. Temperature, 98·4°; pulse 84. Has not vomited to-day. Patient takes fluids well; tongue moist and only very slightly furred. Urine in twelve hours = 16¼ ounces.

*Treatment.*—

4 a.m. Rectal saline with brandy.
4.30 p.m. Rectal saline with quinine, 20 grains.
8.30 p.m. Rectal saline with quinine, 20 grains.

---

1/3/18—10 a.m. Making satisfactory progress. Urine keeping free from hæmoglobin. Temperature normal; pulse 88 per minute. No further vomiting.

6 p.m. Urine still contains a little albumin; amount in twenty-four hours = 30 ounces.

*Treatment.*—Quinine bihyd., 15 grains, t.d.s.

---

2/3/18—9 a.m. Temperature, 98.6° F.; pulse 100. Ol. ricini, 1 ounce given. Urine contains only a slight trace of albumin. Has not vomited his quinine.

6.30 p.m. Temperature, 99° F.; pulse 88. Urine in twenty-four hours = 34 ounces. Taking nourishment well and making steady progress.

10.30 p.m. Temperature, 99·6; pulse 104. Complains of headache.

*Treatment.*—Quinine, 15 grains, t.d.s.

10.30 p.m. An additional 15 grains given. Aspirin, 5 grains.

---

3/3/18—Temperature rising, 100·2° F.; pulse 104. Occasional severe frontal headache; no shivering; tongue slightly furred but moist. Urine in twenty-four hours = 44½ ounces.

*Treatment.*—

11.14 a.m. Intramuscular quinine, 20 grains; pot. citrate, 15 grains, 4-hourly; mist diaphoretic, ½ ounce, 4-hourly.

4.30 p.m. Rectal saline with quinine, 20 grains (retained).

4/3/18—Still complains of headache. Temperature, 99·4° F.; pulse 100. Tongue clean and moist.

*Blood films:* Anisocytosis. Parasites not found.

6 p.m. Temperature, 99·4° F.; pulse 92. Urine in twenty-four hours = 76 ounces. It contains a faint trace of albumin, and some specimens had a fairly heavy deposit of urates.

*Treatment.*—

1 a.m. Quinine, 15 grains, by mouth; pot. citrate and diaphoretic mixture continued; quinine, 15 grains, given four times during the day.

5/3/18—Much improvement. Temperature, 98° F.; pulse 88.

Laboratory Report on urines passed at 6.30 a.m., March 3, 1918: "Practically normal." 7 a.m., March 4: "Urine shows large amount of amorphous deposit (urates), with scanty phosphatic crystals."

6 p.m. Temperature, 99° F.; pulse 88.

Urine in twenty-four hours = 56½ ounces.

*Treatment.*—Mist. diaphoretic and pot. citrat. continued t.d.s.; quinine 15 grains, t.d.s.

6/3/18—Continued improvement. Temperature, 98·4° F.; pulse 88. Marked anæmia.

6 p.m. Temperature, 98·4° F.; pulse 84. Passing a normal amount of urine.

---

9/3/18—Patient had a relapse. Temperature, 101° F.; pulse 100. The relapse was due to a too early reduction of the quinine to 45 grains a day. This amount was not enough to destroy all the parasites in the circulation. The dose was increased to 60 grains a day for a week and no further relapse occurred.

---

16/3/18—Steady improvement.

*Treatment.*—Quinine, 15 grains, t.d.s., to be continued for two months.

*Comments.*—This patient and Corporal M. (Case 6) were admitted on the same day and lay opposite to one another in the same ward.

*Comparison of the Respective Cases.*

| Corporal M. (Case 6). | Private B. (Case 7). |
|---|---|
| Long history of malaria treated with negligible doses of quinine. | Same history. |
| Jaundice: Very marked. | Icteric tinge. |
| Spleen: 1 inch below costal margin; tender. | Spleen: 1½ inches below costal margin; tender. |
| Liver: Slightly enlarged. | Liver: No enlargement. |
| Blood film: Mononuclear increase and benign tertian gametocytes. | Mononuclear increase; no parasites found. |
| Amblyopia after 70 *grains* of quinine a day for two days; this condition only cleared up at the end of about thirty-six hours. | Amblyopia due to the injection of 70 *grains* of quinine in one day; sight became normal in a few hours. |

| | |
|---|---|
| Urine passed in the *nineteen hours* before blindness became evident = 29½ *ounces.* | Urine passed in the *twenty-four hours* before amaurosis occurred = 33 *ounces.* |
| Urine very dark porter colour with much granular debris, epithelial cells and casts. | Dark port-wine colour; deposit same in character but less in amount. |
| Colour of urine returned to normal, but quantity passed gradually diminished until total suppression and death occurred. | Colour also became normal. Daily amount of urine passed in the twenty-four hours was for some days considerably less than 50 ounces a day, but the amount gradually increased and the patient made a good recovery. |

### Quinine Amblyopia in Blackwater Fever.

I have only seen four cases of quinine blindness in ten years' experience of the treatment of malaria. All these occurred in patients suffering from the post-malarial condition known as blackwater fever, and have been reviewed in detail in this chapter.

A report by the consulting ophthalmologist on the cases seen by him in the Salonika Command, which I have in my possession, goes to show that there is little or no change in the acuteness of vision of patients who have recovered from quinine amblyopia. He found the fields of vision to be more or less contracted, and decribes pallor of optic discs and narrowing of retinal arteries in a varying degree in all cases. The contraction of the fields of vision appears to be the most important change

noted. As this is probably only temporary and does not cause the man any inconvenience or affect his efficiency as a soldier, it appears to me to be quite unjustifiable to withhold quinine in blackwater fever because of a possibility of amblyopia occurring. The condition, however, has modified the quinine dosage I use in these cases.

The amount of quinine it is safe to give is governed by the quantity of urine passed in the twenty-four hours immediately prior to the onset of the amaurosis. If the kidneys are unable to excrete sufficient urine to get rid of the quinine, the latter accumulates in the body and gives rise to symptoms of quinine poisoning. As soon as the normal daily amount of urine is again excreted, treatment with larger doses of the drug may be recommenced.

The cumulative effect of quinine in blackwater fever in the acute stage makes it necessary to exercise caution in regard to the amount given while, on the other hand, it is of equal importance to kill the parasites, which are destroying the red blood corpuscles, by giving enough of the drug. We thus have in the same case and at the same time an indication and a contraindication for its administration.

In cerebral and other pernicious types of malaria where there is no difficulty about the excretion of urine, quinine may be given with safety in doses varying from 60 to 120 grains in the space of twenty-four hours. In acute blackwater fever the maximum dose given in a day should not exceed 60 grains, unless more than the normal amount of urine—45 to 52 ounces in twenty-four hours—is being passed.

If the quantity of urine excreted in twenty-four hours is less than 35 ounces there should be a corresponding reduction in the amount of quinine administered daily.

### Scale of Doses recommended in Malarial Hæmoglobinuria and Blackwater Fever.

Quinine bihyd., 20 grains, for the intramuscular, and the same amount in 8 ounces of normal saline solution for the intravenous and rectal injections.

First day. Quinine, 60 grains in twelve hours. Two intravenous and one rectal quinine saline.

Second day. Same; but a rectal quinine saline may be substituted for one intravenous if much improvement has taken place.

Third to fourteenth day. Quinine, 60 grains a day. Two rectal and one intramuscular. If the tongue is quite clean and the urine quite clear, quinine 15 grains four times daily by mouth may be tried on the fifth or sixth day.

The treatment after a fortnight will depend upon the progress made, but the minimum amount should be 45 grains a day for two months following which the dose may be reduced to 10 grains, t.d.s., for another month or two.

Any sign of relapse should be dealt with immediately by increasing the daily dosage of quinine.

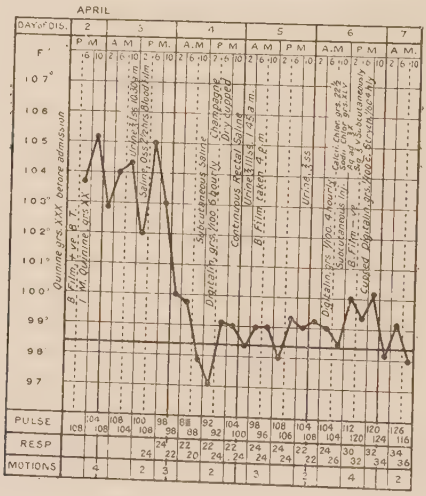
During the convalescent period, mist. arsenic tonic in graduated doses or galyl intravenously may be given in addition to the quinine in order to overcome the anæmia.

*Treatment of Quinine Amblyopia following Blackwater Fever.*—Stop the quinine at once, but as soon as the sight returns recommence with 30 or 40 grains a day for a day or two, after which, if he is passing plenty of urine, increase to 60 grains and continue in the manner laid down above.

*Strychnine.*—I have tried strychnine hypodermically every four hours in cases of quinine amblyopia, but found I got quite as good results without it.

Case 8. Blackwater Fever not treated with Quinine.—I am including the following in this series of blackwater fever cases because the patient was treated without quinine and I had an opportunity of carefully watching the result of such treatment.

Shortly after my experiences detailed above, I was transferred to the — General Hospital to take charge of the medical division there. A week later one of the personnel of the hospital was admitted suffering from blackwater fever. The officer commanding the hospital, after asking




Case 8.

me for my opinion, told me that he did not agree with me and took the case out of my hands. *Although benign tertian parasites had been found in the blood film taken on the previous day he contended that quinine was contra-indicated.* He telephoned to the consulting physician who agreed that quinine should be "severely withheld" because parasites had not been found in a second blood film.

This film was taken at the time I first saw the case, and *after* the patient had received 50 grains of quinine in the preceding twenty-four hours.

COPY OF CASE SHEET—CASE 8 (BY MEDICAL OFFICER OF THE WARD).

Private R., aged 25. Service, 2 years 3 months. Admitted on April 2, 1918.

*Disease.*—Malaria; blackwater fever. Shivering attack on the afternoon of the 1st inst. Temperature, 103° F. in the evening, general pains and headache.

*Blood film:* Positive benign tertian.

Mist. quinine 1 ounce, three doses given.

Malaria: July 1917, September 1917. Some relapses since. On the morning of the 2nd inst. temperature, 99° F. In the evening temperature rose to 105° F. Patient admitted into ward. Vomiting troublesome.

April 3, 1918: Yesterday morning (April 2, 1918), intramuscular quinine 20 grains given. Later patient passed some urine the colour of stout—sent for examination to laboratory. Vomiting persisted throughout the day with varying temperature. Hiccough troublesome. Saline administered *per rectum;* half a pint every 2½ hours. Second blood film negative.

(Seen by the Commanding Officer and Officer in charge Medical Division at 1.30 p.m. on April 3, 1918). No further quinine administered.

April 4, 1918: Patient has passed no urine since yesterday afternoon. Had a restless night with vomiting. Has retained salines fairly well, for about an hour each time. On examination, tongue furred. Heart sounds good. Spleen ++ palpable, slightly tender. Skin and conjunctivæ, icterus. Dry cupped, hot fomentations to loins. Subcutaneous salines with sodii bicarbonate. Digitalin, 100 grains six-hourly hypodermically.

April 5, 1918: General condition shows little change this morning; he had a fair night with some sleep.

Occasional vomiting, but has taken a considerable quantity of fluids. Continuous rectal salines, three pints retained. At 1.45 this morning patient passed urine 3½ oz. the colour of stout. Tongue furred, rather dry. Pulse fair volume.

April 6, 1918: Patient exhibits no improvement. ½ ounce of urine in last twenty-four hours. Little vomiting. Taken fluids well; salines retained fairly well. Jaundice increased. Pulse-volume not so good.

Patient was seen by Assistant Consulting Physician yesterday, who recommended continuance of present treatment.

*Blood film:* Negative. Digitalin, $\frac{1}{100}$ grain four-hourly. Calcium chlor. 22½ grains, sodii chlor. 40 grains, aq. dist. 10 ounces—5 ounces subcutaneously.

April 6, 1918: 4 p.m., pulse more rapid, quality failing. No vomiting. Taking nourishment fairly well; retaining all salines. 6 p.m., dry cupped. Digitalin and strychnine four-hourly hypodermically.

April 7, 1918: Patient markedly worse. Has not passed urine. Had a fair night. Pulse now rapid, low tension. Temperature, 99° F. Returns salines. No vomiting nor hiccough. Has attacks of palpitation. Drowsy yet restless at times. Spleen, 1½ inches below costal margin on deep inspirations, not particularly tender. Died at 1.40 p.m. on April 7, 1918.

*Notes by Author.*—When seen by me on April 3, 1918, his condition was as follows: Conjunctivæ very jaundiced. Skin icteric. Spleen, 1½ inches below costal margin. Vomiting. Hiccough very distressing. Had passed stout-coloured urine two hours before.

On account of the history, positive blood film and general condition, I suggested that 60 grains of quinine should be given within the next twenty-four hours as

patient was seriously ill and it was his only chance of recovery.

Forty-eight hours later he passed 3½ ozs. of urine. His spleen was then 2½ inches, actual measurement, below the costal margin, the jaundice had increased and he was still vomiting.

Patient died on the fourth day having received no quinine during this period.

*Post-mortem.*—An autopsy was made, at my request, by the bacteriologist of the hospital, and we found: Heart dilated; muscle pale; right side, walls very much thinned; left side, walls thinned. Lungs normal. Right kidney normal, 5 ounces in weight; left kidney rather enlarged, 6½ ounces; section of kidney brownish colour, with darkly stained areas due to deposition of pigmented granules in the convoluted tubules. Liver enlarged, 66 ounces, fatty appearance. Spleen three times normal size, 14½ ounces; chocolate coloured and very soft, *typically malarial.* Bladder very much contracted.

*Comments.*—(1) I sent in my resignation as officer in charge of the medical division of the hospital and was sent to the Front as an M.O. to a field ambulance.

(2) A fortnight later at a lecture on Blackwater Fever, by the Consulting Bacteriologist of the Salonika Forces held at the — Casualty Clearing Station, I gave details of this case and asked the lecturer what treatment he would have used under the circumstances. His reply was, "*I would have given quinine of course.*"

### Redwater Fever (Malarial Hæmoglobinuria).

I have termed this "redwater" in order to differentiate it from blackwater fever. It is a mild form of the latter condition, in which the colour of the urine varies from

a light to a darkish red, but never becomes dark port-wine or stout coloured.

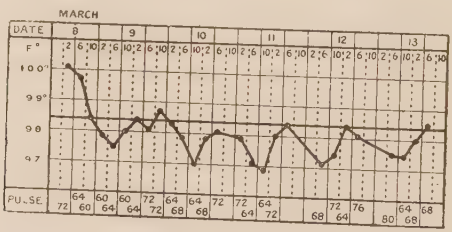
The deposit is scanty and differs from the debris found in blackwater fever urine in its microscopic characters.

In redwater fever we see the epithelial cells from the convoluted tubules of the kidney filled with granular deposit and there is very little, if any, *free* granular debris.

In blackwater fever the earlier specimens show large amounts of *free* granular deposit and few epithelial cells, while in the very acute stages the precipitate consists of numerous stripped epithelial cells, but less granular deposit.

Case of Pte. P., aged 40. Service, two years. Admitted on March 7, 1918. In Balkans, 1 year 8 months.

*Previous History.*—Malaria (—General Hospital) October, 1917, and three relapses since, treated in camp; $2\frac{1}{2}$ months off duty since middle of October, 1917.




Case. Private P.

*Onset of present illness:*—Four days before admission with headache, pain in the legs and back, shivering and jaundice (conjunctivæ).

*On admission.*—Temperature, 101·5° F.; pulse 120; tongue, furred and moist; eyes, slightly injected, deeply jaundiced; herpes, slight, circumoral; skin, jaundiced, slight; heart, 120 per min., regular, sounds weak, no bruit present; lungs, nil; spleen, plus and very tender.

*Treatment.*—Calomel 5 grains on admission; quinine sulph., 15 grains, t.d.s.

*Blood films:* Parasites not found.

8/3/18—Hæmoglobinuria. Patient passed urine of a brownish-red colour rather lighter than port-wine, obviously containing hæmoglobin. Temperature, 100·2; pulse, 72, regular, good volume; jaundice, conjunctivæ deeply stained, skin less so; anæmia; spleen, palpable, less tender.

*Further History.*—Patient says that he has noticed his urine has been coloured with blood each day for the last four days.

*Daily amount of Quinine taken since October last.*

October 11, to November 4, 1917: 40 grains for nine days, 30 grains for eight days, 10 grains for eight days.

November 5, to November 25, 1917 (twenty-one days): 15 grains a day.

November 27, 1917, to February 2, 1918 (sixty-eight days): 10 grains a day. February 19, to March 4, 1918 (two weeks): one dose daily, amount unknown.

On March 4, 1918, patient says his quinine was stopped and he was put on to a tonic medicine; he noticed the change in his urine on that day.

Laboratory report on specimen of urine passed this morning: "Oxalate crystals; large epithelial cells from urinary tract, several being filled with granular debris; granular casts; very little free granular debris."

*Treatment.*—

12 noon. Rectal saline, 10 ounces, with quinine, 20 grains.

2 p.m. Intramuscular quinine, 20 grains.

2.20 p.m. Passed 17½ ounces of urine of a dark orange colour (much less red than previous specimen) and slightly muddy.

*Treatment.*—6 p.m. Quinine bihyd., 20 grains, by mouth.

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Patient taking fluids well; no vomiting; tongue clean and moist. Urine passed this evening shows further slight improvement. Total amount of urine from admission to this ward (11.45 a.m.) to 7 p.m. = 33 ounces.

*Treatment.*—10.30 p.m. Quinine bihyd., 15 grains, by mouth.

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Laboratory Reports on Urines—March 8, 1918. 2.20 p.m.: Granular deposit; epithelial cells from urinary tract; casts (few). 5 p.m.: Very little deposit; no cells nor casts. 6.30 p.m.: Deposit not markedly granular. 7.45 p.m.: Very numerous epithelial cells—many definitely renal in origin; several engorged with granular debris; granular and epithelial casts (numerous); very little free granular debris.

9/3/18—Temperature 98° F.; pulse 60; tongue moist and clean. Has taken fluids well during night, only vomited once, slightly, at 4.45 a.m. Marked anæmia; jaundice *slightly* less. Total twelve hours quantity of urine, 7 p.m. to 7 a.m., = 46 ounces.

*Treatment.*—Brandy, ½ ounce, four-hourly.

10.30 a.m. Quinine bihyd., 20 grains.
1 p.m. Quinine bihyd., 15 grains.
2 p.m. Rectal saline with quinine, 20 grains.
5.45 p.m. Intramuscular quinine, 20 grains.

---

Gradual improvement in appearance of urine during the day; successive specimens being lighter in colour and containing less hæmoglobin.

Patient vomited twice to-day, at 3.30 p.m. and 6.45 p.m., his tongue being slightly furred; vomit contained a fair quantity of bile.

Evening: Temperature 98·2° F.; pulse 72. Patient feeling much better. Total twelve hours urine, 7 a.m. to 7 p.m. = 41½ ounces.

Laboratory Reports on Urines.—March 9, 1918, 3 a.m.: "Epithelial cells engorged with granular deposit." 11.50 a.m.: "Granular casts. Little free deposit." 10.40 p.m.: "More cells, some definitely from bladder, some from kidney."

10/3/18—Temperature 97·8° F.; pulse 68. No vomiting during night; urine apparently now free from hæmoglobin; jaundice much less marked; very anæmic. Total twelve hours quantity of urine, 7 p.m. to 7 a.m. = 40½ ounces.

*Treatment.*—Quinine bihyd., 15 grains, t.d.s.

2.45 p.m. Rectal saline, 10 ounces with quinine, 20 grains.

Evening. Temperature 98·2° F.; pulse 72. Has not vomited to-day. Total twelve hours quantity of urine, 7 a.m. to 7 p.m. = 39 ounces.

11/3/18—Temperature 97·2° F.; pulse 64. Jaundice less. Total twelve hours quantity of urine, 7 p.m. to 7 a.m. = 36 ounces. Urine remains free from hæmoglobin, but still contains a little albumin.

Laboratory Reports on Urines.—March 10, 1918, 2.30 p.m.: "Large number of epithelial cells mostly engorged with granular debris, some clear. Several are very large in size—bladder cells, others definitely from kidney. Epithelial and granular casts few. *Small amount of free* deposit." 9 p.m.: "Similar to above, but all epithelial cells containing granules." March 11, 1918, 6.30 a.m.: "Practically normal."

*Treatment.*—Quinine bihyd., 15 grains, 4 times daily.

Evening. Improvement maintained. Temperature, 98·4° F.; pulse 72. Total twelve hours urine, 7 a.m. to 7 p.m = 48½ ounces.

12/3/18—Temperature, 97·4° F.; pulse 72. Patient doing well; only slight icteric tinge in conjunctivæ now. Urine, trace of albumin. Total twelve hours quantity, 7 p.m. to 7 a.m. = 30 ounces.

15/3/18—Twenty-four hours urine, 7 a.m. to 7 a.m. = 93 ounces. Contains no albumin.

16/3/18—Twenty-four hours urine = 85 ounces. Patient making good progress; improved in every way.

*Treatment.*—Quinine bihyd., 15 grains, 4 times daily still continued.

17/3/18—Twenty-four hours urine = 76½ ounces. No further rise of temperature or relapse.

18/3/18—Continued improvement.

19/3/18—Quinine reduced to 15 grains, t.d.s.

25/3/18—Marked improvement. No rise of temperature during last week. Anæmia much improved. Patient able to be up for a short time to-day.

30/3/18—Evacuated by hospital ship to England.

*Comments.*—(1) The history of malaria with frequent relapses, insufficiently treated with quinine, is very characteristic.

(2) The epithelial cells are reported to have been engorged with granular deposit, while there was very little free granular debris present. This case resembles that of Private B. (Case 7, Blackwater Fever), but in the latter, the urine was much darker in colour and there was less engorgement of the epithelial cells.

I look upon the case of Private B. as being on the

border line between, but more a blackwater fever than a redwater fever.

The study of the urines in all these cases is very interesting in as much as it shows the stages by which untreated malarial hæmoglobinuria may gradually pass into true blackwater fever.

The treatment of redwater fever is the same as that of blackwater fever, and like it, depends on the virulence of the malarial attack (see p. 229).

## CHAPTER XI.

## POST-MALARIAL NERVOUS MANIFESTATIONS.

It is of great importance to remember, when called upon to treat patients suffering from obscure nervous lesions, who have resided in malarial countries, that the effects of the disease on the central nervous system and the peripheral nerves generally are many and varied.

A few notes on some of these cases may not be out of place.

Case 1. *Malarial Tremor.*—Private C., aged 29 years 9 months. Admitted on October 12, 1917. In Balkans since 1915. Malaria in July, 1917.

*Onset of present illness:*—Six days ago. Headache, backache, vomiting.

*On admission.*—Patient is in a peculiar nervous condition, and it is very difficult to obtain answers from him; marked tremor of hands; tongue very furred and very marked tremor. When asked to protrude it, the tongue darts forwards and back again in a sharp, jerky, tremulous fashion. Heart and lungs normal; spleen plus.

Seen by Colonel Purves Stewart, Consulting Physician, who diagnosed the case as one of malarial tremor.

*Treatment.*—Quinine, 15 grains, t.d.s., and intramuscular quinine, 20 grains daily, for four days.

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16/10/17—Has had no pyrexia; tremor and pulse have improved on the quinine (65 grains a day); intramuscular quinine discontinued; quinine, 15 grains, t.d.s., given.

30/10/17—Steady improvement, tremor disappearing; mist. arsenic tonic commenced; quinine sulph. reduced to 30 grains a day.

CASE 2. *Malarial Tremor.* — Private S., aged 21. Service, 2 years 2 months. Admitted on January 29, 1918.

*Previous History.*—Malaria; ten relapses; five times in hospital.

*Onset of present illness:*—January 23, 1918 (— General Hospital).

*Symptoms.*—Rigor and sweating; very anæmic.

*On admission* (28th General Hospital).—Heart normal; spleen plus.

*Treatment.*—Quinine sulph., 10 grains, t.d.s.

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30/1/18—Tremor of eyes, tongue and hands; no headache; knee-jerks normal; patient nervous and excitable, but says he feels well.

31/1/18—Knee-jerks brisk; ankle-jerks not elicited.

*Treatment.*—Quinine stopped; pot. brom., 20 grains.

*Blood film:* No parasites found.

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1/2/18—Transferred to cerebral ward; general condition good; tongue clean and moist. Eyes: sharp lateral movement of eyeballs, not a true nystagmus; when animated the twitching involves head and neck. Tremor marked when patient is excited, but it is not troublesome if he is left alone.

*Treatment.*—Quinine, 15 grains, four times a day.

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2/2/18—Vomited during the night; tongue slightly furred; temperature, 97° F.; pulse 84; twitching and tremor about the same.

*Treatment.*—Quinine by mouth stopped.

Noon. Intramuscular quinine, 20 grains.
6 p.m. Intramuscular quinine, 20 grains.
11 p.m. Intramuscular quinine, 20 grains.

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3/2/18—Temperature, 97° F.; pulse 80; patient feels a little better; knee-jerks brisk and equal; no ankle-jerks; plantar reflexes flexor, very slight; when up, patient is unable to stand except with feet some distance apart, the tremor affecting the whole body. He is very ataxic; no tremor if patient is left quiet, and less in the night than in the light; has noticed no loss of vision; speech jerky, but not syllabic; occasional vomiting after a period of nausea.

*Treatment.*—

12 noon. Intramuscular quinine, 20 grains.
6 p.m. Intramuscular quinine, 20 grains.

Seen by Assistant Consulting Physician, who regarded the condition as functional and recommended isolation. Transferred to Hospital for Nervous Diseases as a "post-malarial nervous condition."

*Comments.*—I have seen a number of other cases of tremor similar to the foregoing, all of which recovered when the general malarial condition was efficiently treated with quinine.

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CASE 3. *Malaria, Recurrent—Myoclonus.*—Private J. Admitted on September 26, 1917. In Balkans, 1 year 3 months.

*Previous History.*—Malaria in August, 1917.

*Onset of present illness:*—Seven days ago.

*Symptoms.*—Headache, shivering, sweating, vomiting, constipation, dizziness and abdominal pain.

*On admission.*—Complained of malaise; temperature, 100° F.; pulse 114; tongue moist; eyes injected and jaundiced; herpes labialis; heart and lungs normal; spleen soft, palpable and tender; abdomen, tenderness in right iliac fossa; clonic contraction of left arm. States that he has had this previously when suffering from malaria.

*Treatment.*—Calomel and mag. sulph.; quinine 10 grains, t.d.s.

28/9/17—*Notes by Colonel Purvis Stewart:* "As he lies in bed he shows a rapid, irregular clonic spasm chiefly in the pectoral muscles frequently adducting the shoulders, but often contracting without producing any joint movement. Spasm more marked in left pectoral than in right. In addition, occasional myoclonus in abdominal muscles, hardening the anterior abdominal wall and sometimes jerking the body forwards. A slight clonic spasm in left biceps and triceps, none in wrist or fingers. Patient states that the condition started during malaria five weeks ago, and ceased when he recovered. The movements cease during sleep. They were very pronounced when the patient woke this morning and found the medical officer at the bedside watching him."

2/10/17—Patient's temperature has been normal for three days, and the spasms have now totally disappeared.

---

CASE 4. *Malaria and Peripheral Neuritis.*—Lance-Corporal S., aged 48. Admitted on November 15, 1917.

In Balkans, 2 years. Malaria in April, 1916, and four times since.

*Onset of present illness:*—Five days ago. Shivering, headache and sweating. Three days ago, difficulty in walking, numbness of feet. No history of sore throat or alcohol.

*Notes by Col. Purves Stewart:* "First noticed difficulty in walking. Next morning could only walk with support. Weakness of legs since increased; at same time as weakness of legs difficulty in dorsiflexing wrists; no sphincter trouble. Notices deficient sensation below knees, aching above knees, similar pains in upper half of forearms. Speech and articulation normal. Pupils and cranial nerves normal. To cotton-wool loss of sensation in forearm up to elbow extensor, and up to middle of forearm on flexor aspect. In lower limbs anæsthesia to middle of thighs. Zone of anæsthesia only on front of chest from third rib to 1 inch below ziphisternum. To pin pricks analgesia of upper limbs from elbows downwards. No analgesia of trunk. Lower limbs, analgesia up to middle of thighs. Joint sense normal in upper limbs, severely impaired in lower limbs, feeble at all joints especially extensors of wrists, but no individual movement impossible. No muscle tenderness. Abdominal muscles contract, but he cannot sit up without assisting himself with his hands. Lower limbs more severely paralysed and flaccid. Dorsiflexors of ankle especially feeble, but not absolutely paralysed, i.e., they can contract but not enough to move joint. Cannot lift either limb off bed against gravity. Severe pains in knee-joints on passive movements, but no joint swelling. Supinator-jerks, knee-jerks and ankle-jerks alert; plantars absent; abdominals absent. Heart sounds inaudible; pulse 75 per minute. Lungs, few ronchi at bases posteriorly,

but no dulness. Spleen palpable 1 inch below costal margin."

Urine alkaline, specific gravity, 1030; no albumin; no sugar.

*Treatment.*—Tinct. nucis vom., 10 minims, t.i.d., increased by 1 minim per dose each day; tinct. digitalis, 10 minims, t.d.s.

20/11/17—Slept well and says he feels better.

21/11/17—Bad night. Is extremely weak; cyanosed; has a short cough, but cannot clear his throat; pulse very poor. Brandy 1 ounce every four hours. Died at 11.45 a.m.

*Post-mortem Report.*—Brain: Normal.

Cord: Externally apparently normal.

Lungs: Bound down to chest wall and diaphragm by old adhesions; some bronchitis with emphysema, especially at bases; no nodules observed.

Heart: Normal.

Liver: Slightly enlarged and congested.

Spleen: Somewhat enlarged, firm in consistence, slightly fibrotic.

Kidneys and intestines: Normal.

Brain, spinal cord, part of spleen, a section of sciatic, musculo-spiral and phrenic nerves excised and sent for examination to the base laboratory.

*Base Laboratory Report on Sections of Tissues.*—Spleen: Stroma increased. Malpighian bodies show some necrotic change. Malarial pigment present in small quantity. No parasites seen.

Brain: Congested. No degeneration in cells. No malarial parasites seen.

Cord: Three sections examined from different levels: all show an area to the right postero-lateral area of the central canal, which is infiltrated with cells mostly

lymphatic in type. The cells of the cornua show marked degeneration, some cells being completely degenerated.

Nerves: Some interstitial increase between the bundles; the myelin sheaths show marked degeneration. Many of the axis cylinders show complete degeneration.

CASE 5.—*Malaria (Malignant Tertian) and Right Brachial Neuritis.* Pte. B., aged 32. Service, two years. Admitted on October 10, 1917. In Balkans, 1 year 1 month. Had malaria in August, 1917.

*Onset of present illness:*—Four days ago. Shivering; sweating; headache; aching pains all over body; vomiting.

*Blood film:* Malignant tertian.

*Notes from Casualty Clearing Station.*—"Attack of violent delirium on the night of October 8, 1917; passed off next day."

*On admission.*—October 10, 1917. Eyes, some injection of conjunctivæ; tongue furred, rather dry; heart normal; pulse regular; spleen not palpable, slightly tender.

*Treatment.*—Patient given an intramuscular of quinine on admission on account of dirty tongue. Rather wild staring appearance, and history of cerebral symptoms. Quinine, 15 grains, t.d.s., daily.

11/10/17—Patient much better. Quiet night. Temperature normal.

13/10/17—Patient complains of occasional pain, numbness and inability to use fully the right upper arm and shoulder. He is unable to push the arm and hand directly forward with elbow flexed, the arm becoming rotated inwards with the hand to the body—the same movement a boxer makes when bringing off the "kidney punch." No pain or stiffness on passive movement. Patient

unable to raise arm and hand above shoulder or to back of neck. Area of anæsthesia over back of right shoulder. Some wasting, especially of scapular muscles.

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19/10/17—*Notes by Colonel Purves Stewart:* "Right arm is habitually tonically semiflexed at elbow; he does not swing that arm when walking. Pupils and cranial nerves normal. To light touches, anæsthesia over right deltoid area. To pin pricks, analgesic area in same region but less extensive. Right trapezius much more feeble than left. Cannot shrug right shoulder at all. Considerable pain on passive abduction of shoulder joints. Contracts right deltoid, but not enough to move the joint. Biceps very feeble, triceps better. All muscles of right shoulder and elbow feeble. Both latissimi contract on coughing. Slight wasting of supra- and infra-spinators. Supinator-jerks brisk and equal. Tenderness on pressure above and below right clavicles and over brachial plexus. Knee-jerks brisk and equal."

*Comments.*—These notes may be of some value as a guide in the diagnosis and treatment of neuritis and other nerve conditions occurring in persons returning from one or other of the various malaria-stricken fronts.

After the war the general practitioner in England and the Dominions will be faced with a number of problems which will be very difficult to solve, and unless he realizes at the outset what complications are to be expected during and after attacks of malarial fever, it

is reasonable to suppose that many discharged soldiers will be ruined in health and valuable lives imperilled or lost.

Another point which should not be lost sight of is that medical officers who have served only in France or at home will be at a great disadvantage in competition with those who have had the fortune or misfortune to serve in Macedonia, Mesopotamia, or East Africa.

3. Stegomyia Mosquito.

(See p. 5.)

Facc p. 248

## CHAPTER XII.

## CONCURRENT DISEASES AND DIFFERENTIAL DIAGNOSES.

### Malaria and Appendicitis.

What is known as "Malarial Appendicitis" has been described, and many experienced physicians and surgeons in the Balkans regard this as a definite entity.

It is thought that the malarial parasite causes appendicitis because the abdominal symptoms often disappear after treatment with quinine.

The case on admission usually presents the following symptoms: Pain, tenderness and some rigidity in the right iliac fossa. There may or may not be a rise of temperature and an increase in the pulse-rate.

The blood film may be positive, and the spleen enlarged and tender.

A total and differential leucocyte count, if they show a definite increase, are of value as an indication for operation, but a normal count does not exclude the possibility of an acute appendicitis.

If the hypothesis is accepted that the pain and tenderness are due to the malaria, then the question of operation is a very difficult one. If, on the other hand, as I believe, the abdominal condition is due to an ordinary attack of appendicitis in a person suffering from malaria, there should be no hesitation about performing a laparotomy. I consider from the experience I have had in these cases that malaria, by lowering the resistance of

the body, increases the liability of the various organs to attacks of an inflammatory nature and that this is more likely to occur in the appendix on account of its poor vascular supply than anywhere else.

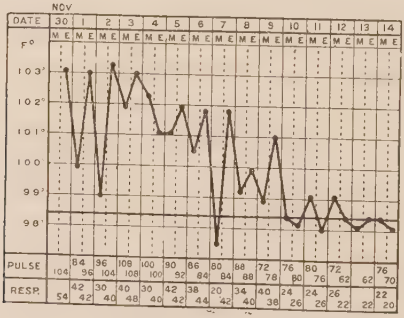
My advice is to operate at once if there is the slightest doubt in regard to the cause of an acute abdominal condition.

Treat the malaria with quinine by all means, but do not by waiting, run the risk of finding at a later date a gangrenous appendix in an abdomen full of pus.

Some observers describe a referred pain in the region of the appendix which they say is due to gastro-splenic or gastro-hepatic adhesions. This, however, appears to me to be highly problematical.

### Pneumonia and Malaria.

Case.—Greek driver, aged 22. Service, six months. Admitted on November 30, 1917. In Balkans all his life




Greek Driver.

*Report from Field Ambulance.*—"Temperature, 102·2° F.; pulse 120; dyspnœa; spleen not felt; congestion at bases and râles all over chest; blood-stained sputum; no vomiting."

*Report from Casualty Clearing Station.*—"Temperature,

103° F.; pulse 136; respirations 54; spleen enlarged; patches of congestion in both lungs."

*On admission* to this hospital.—Temperature, 103° F.; pulse 104; respirations 54; conjunctivæ slightly congested and injected; tongue, moist and clean; spleen enlarged, tender; left lung, greater part is dull posteriorly; breathing very harsh, expiration prolonged, bronchial breathing especially pronounced above level of eighth rib behind; high-pitched rhonchi and fine crepitations at both bases; vocal resonance not definitely increased; heart, slight systolic mitral not propagated; sputum copious, frothy, and not blood-stained.

*Blood film:* Type undetermined; mononuclears in excess with ingested pigment.

*Treatment.*—Intramuscular quinine 20 grains; strychnine, $\frac{1}{60}$ grain; digitaline, $\frac{1}{100}$ grain hypodermically four-hourly.

Mist. creosote :—

| | | |
|---|---|---|
| ℞ | Creosote ... ... ... | ♏ iii. |
| | Pot. iod. ... ... ... | gr. v. |
| | Tinct. digitalis ... ... | ♏ v. |
| | Tinct. nucis vom. ... | ♏ iv. |
| | Ext. glycrrh. liq.... ... | ʒi. |
| | Aq. camph. ad ... ... | ʒss. |

Sig. ½ ounce every four hours.

---

1/12/17—10 a.m. Temperature, 99·8° F.; pulse 84; respirations 42; spleen still very tender; cough paroxysmal; sputum still blood-stained.

6 p.m.—Temperature, 103° F.; pulse 96; respirations 42.

*Treatment.*—Quinine, 15 grains, t.d.s., by mouth; intramuscular quinine, 20 grains. Cardiac tonics as before.

2/12/17—a.m. Temperature, 99° F.; pulse 96; respirations 30; spleen less tender; liver slight tenderness, no increased dulness; cough and sputum, no change.

p.m. Temperature, 103·2° F.; pulse 104; respirations 40.

*Treatment.*—Quinine, 15 grains, t.d.s., by mouth. Cardiac tonics as before.

---

3/12/17—a.m. Temperature, 102° F.; pulse 108; respirations 40. Temperature is continuous in type; patient rather drowsy; cough and sputum improving; crepitations in lower half of left lung, and at right base; spleen and liver less tender.

p.m. Temperature, 103° F.; pulse 108; respirations 48.

*Treatment.*—Same as yesterday, with intramuscular quinine, 20 grains, in addition.

---

4/12/17—a.m. Temperature, 102·2° F.; pulse 100; respirations 30. Slept well; prune juice sputum; leucocyte count, 6,000 per c.mm.

p.m. Temperature, 101° F.; pulse 100; respirations 40.

*Treatment.*—Same but no intramuscular injection.

---

5/12/17—a.m. Temperature, 101° F.; pulse 90; respirations 42. Patient slightly improved, but pulse is still rather rapid and feeble.

p.m. Temperature, 101·8° F.; pulse 92; respirations 42.

*Treatment.*—Quinine, 15 grains, t.d.s., and cardiac tonics continued.

---

7/12/17—a.m. Temperature, 97·6° F.; pulse 80; respirations 20. Patient's temperature fell to below normal this morning, but rose again in the evening.

p.m. Temperature, 101·8° F.; pulse 84; respirations 42.

*Treatment.*—As before.

---

10/12/17—Temperature has been irregular during the last three days; rises are probably due to malaria.

---

13/12/17—a.m. Patient much improved; has only had slight rises of temperature to 99° F.; spleen still palpable and tender.

p.m. Temperature, 98·4° F; pulse 62; respirations 22.

*Treatment.*—Quinine, 15 grains, t.d.s., and mist. creosote still continued, but subcutaneous injections of digitaline and strychnine stopped.

---

*Comments.*—The interest in this case lies not only in the amount of quinine given, but also in the degree of cardiac stimulation necessary.

It must be remembered that the heart muscle of a chronic malarial patient is much weakened and requires considerably more treatment than is the case in a straightforward pneumonia.

The method of treating the malaria with 60 grains of quinine a day, and at the same time stimulating the heart with both subcutaneous injections and cardiac tonics by mouth has proved very successful.

When I was attached to a Serbian hospital during the winter of 1916-17, we found that the mortality from malaria complicated by pneumonia was out of all proportion, and

it was not until we came to realize the necessity for vigorously treating both conditions that our results were satisfactory.

The swing of the temperature before the crisis, on the eighth day, was a quinine effect on an ordinary pneumonia temperature. The fluctuations afterwards were due to the malaria. An intramuscular or rectal saline with quinine on the first couple of days after the crisis would in all probability have prevented the temperature rising above normal.

Malaria complicated by Dysentery.—What has been termed "malarial mucous colitis" is a condition in which blood and mucus appear in the stools of a patient suffering from malaria. It is probably a true dysentery and not the effect of the malaria parasites on the mucous membrane of the intestines—a theory I have heard propounded.

The bacilli of Shiga and Flexner and the amœba, may or may not be found, a negative result does not necessarily mean that they are not present.

Most men living in tropical countries are "carriers" of the dysentery organism, and when the system becomes lowered by attacks of malaria, it makes its presence felt.

The dysenteric condition is generally a mild one and the blood and mucus quickly disappear from the stools on treatment with sodium sulphate—3i every hour—if quinine is given as well to counteract the malaria.

*Hospital dysentery* is a name given to dysentery which may appear weeks after a patient has been admitted to hospital. It usually occurs in cases of severe malaria. We have had very little trouble with this condition compared with other hospitals, due, I consider, to the vigorous quinine and arsenic treatment to which the patients are subjected here.

The Enteric Group of Fevers and Malaria.—The

differential diagnosis is generally simple. A continuous temperature which has not yielded to quinine by the fourth day should be regarded with suspicion. Blood should at once be taken and sent to the laboratory for culture and also for a Widal test. If both are negative, a "rising Widal" should be tried for, that is, the test should be repeated on the fifth and tenth days following. If both these are negative, T.A.B. may be excluded. The effect of recent inoculation with the T.A.B. vaccine on the Widal reaction should be borne in mind and duly discounted. In these cases the first Widal test is generally inaccurate on account of the high results obtained; these are due to the protection given by the inoculation.

*Technique for taking Blood for Blood Culture and Widal Reaction.*—The needle of a sterilized 10 c.c. syringe is introduced with aseptic precautions into a suitable superficial vein on the anterior aspect of the forearm, the vein being distended first by means of a tourniquet or bandage round the upper arm. Fill the syringe with blood and immediately transfer the contents into a large sterile test-tube containing a suitable liquid medium. This is then incubated at blood heat in the laboratory and examined daily for three days. If, at the end of this period, the culture is sterile, the test is negative. When taking blood for a culture run some of it into a Wright's capsule, seal the ends in a flame and send it to the laboratory for the purpose of having a Widal test done as well.

*Widal Reaction.*—The small amount of blood required for this is *usually* obtained by pricking the finger or the lobe of the ear with a sterile needle. Before taking blood, swab the surface of the skin with alcohol, ether or iodine. Positive results are not as a rule got *until* the seventh or eighth day. *Blood culture* is only of value in diagnosis if the serum is obtained *before* the seventh day of the fever. After this, results are invariably *negative*.

*Cultivation of the Bacillus from the Stools.* — Some authorities regard this as the most accurate method of arriving at a diagnosis in enteric and the paratyphoid fevers.

Coma.—The use of (*a*) Large doses of quinine, (*b*) lumbar puncture, in the differential diagnosis of cases of semi-coma and coma is, as I have already stated, of the utmost value.

*Final Remark.*—If attention is paid to the various points I have endeavoured to emphasize, I feel convinced that much success will be attained in the treatment of malarial fever and its complications.

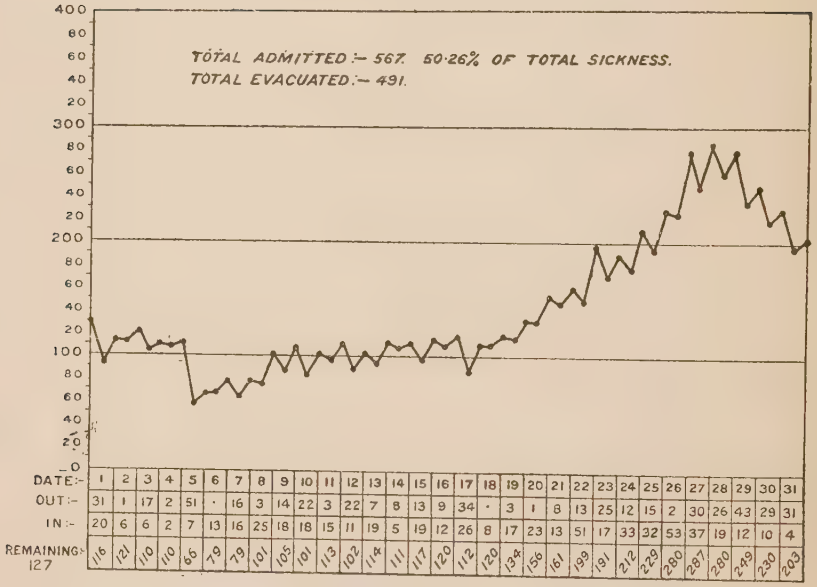
# APPENDIX.

## MALARIA IN MACEDONIA.

### (*Charts for Twelve Months.*)

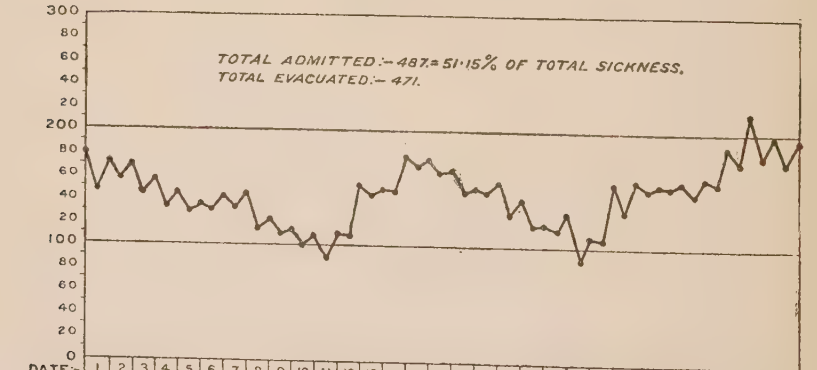
Charts showing the daily number of cases of malaria admitted to the 28th General Hospital during the twelve months ending February 28, 1918.

## Malaria, March, 1917.



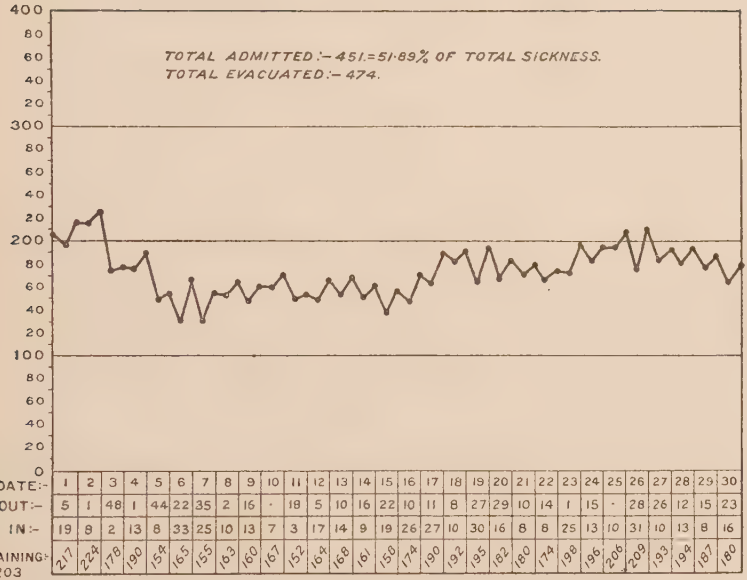

| DATE:— | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OUT:— | 31 | 1 | 17 | 2 | 51 | · | 16 | 3 | 14 | 22 | 3 | 22 | 7 | 8 | 13 | 9 | 34 | · | 3 | 1 | 8 | 13 | 25 | 12 | 15 | 2 | 30 | 26 | 43 | 29 | 31 |
| IN:— | 20 | 6 | 6 | 2 | 7 | 13 | 16 | 25 | 18 | 18 | 15 | 11 | 19 | 5 | 19 | 12 | 26 | 8 | 17 | 23 | 13 | 51 | 17 | 33 | 32 | 53 | 37 | 19 | 12 | 10 | 4 |
| REMAINING:— 127 | 116 | 121 | 110 | 110 | 66 | 73 | 73 | 101 | 105 | 101 | 113 | 102 | 114 | 111 | 117 | 120 | 112 | 120 | 134 | 156 | 161 | 199 | 191 | 212 | 223 | 280 | 287 | 280 | 249 | 230 | 203 |

## May, 1917.



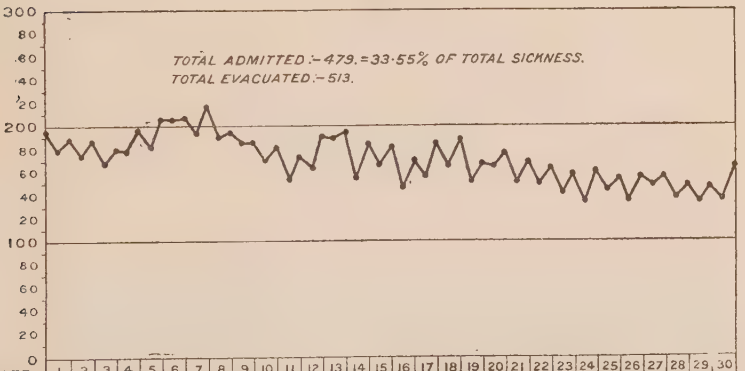

| DATE:— | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OUT · | 32 | 12 | 23 | 23 | 18 | 6 | 10 | 28 | 11 | 13 | 23 | 2 | 10 | 1 | 9 | 12 | 18 | 4 | 29 | 21 | 4 | 40 | 4 | 25 | 11 | 1 | 10 | 5 | 14 | 38 | 14 |
| IN:— | 23 | 8 | 12 | 13 | 9 | 10 | 12 | 6 | 3 | 10 | 23 | 45 | 4 | 33 | 5 | 1 | 4 | 9 | 14 | · | 12 | 22 | 50 | 28 | 4 | 4 | 15 | 33 | 44 | 9 | 22 |
| REMAINING:— 180 | 171 | 167 | 156 | 146 | 137 | 141 | 143 | 121 | 113 | 110 | 110 | 153 | 147 | 179 | 175 | 164 | 150 | 155 | 140 | 119 | 127 | 109 | 155 | 156 | 151 | 154 | 159 | 187 | 217 | 188 | 196 |

## April, 1917.



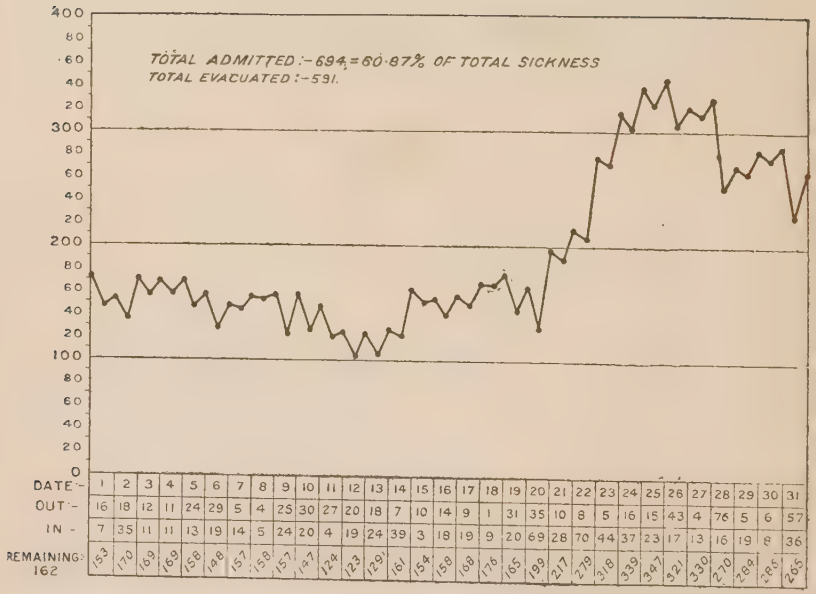

| DATE:— | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OUT:— | 5 | 1 | 48 | 1 | 44 | 22 | 35 | 2 | 16 | · | 18 | 5 | 10 | 16 | 22 | 10 | 11 | 8 | 27 | 29 | 10 | 14 | 1 | 15 | · | 28 | 26 | 12 | 15 | 23 |
| IN:— | 19 | 8 | 2 | 13 | 8 | 33 | 25 | 10 | 13 | 7 | 3 | 17 | 14 | 9 | 19 | 26 | 27 | 10 | 30 | 16 | 8 | 8 | 25 | 13 | 10 | 31 | 10 | 13 | 8 | 16 |
| REMAINING 203 | 217 | 224 | 178 | 190 | 154 | 165 | 155 | 163 | 160 | 167 | 152 | 164 | 168 | 161 | 150 | 174 | 190 | 192 | 195 | 182 | 180 | 174 | 198 | 196 | 206 | 209 | 193 | 194 | 187 | 180 |

## June, 1917.




| DATE: | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OUT:— | 17 | 14 | 19 | 2 | 16 | 1 | 13 | 27 | 9 | 14 | 26 | 11 | 2 | 39 | 20 | 33 | 14 | 18 | 35 | 4 | 24 | 22 | 21 | 24 | 18 | 20 | 7 | 17 | 15 | 11 |
| IN:— | 8 | 12 | 13 | 20 | 24 | 1 | 24 | 4 | · | 10 | 19 | 29 | 6 | 27 | 18 | 22 | 27 | 22 | 15 | 12 | 18 | 15 | 17 | 26 | 12 | 21 | 7 | 9 | 13 | 28 |
| REMAINING 196 | 187 | 185 | 179 | 197 | 205 | 205 | 216 | 193 | 184 | 180 | 173 | 191 | 195 | 183 | 181 | 170 | 183 | 187 | 167 | 175 | 169 | 162 | 158 | 160 | 154 | 155 | 155 | 147 | 145 | 162 |

MALARIA, JULY, 1917.



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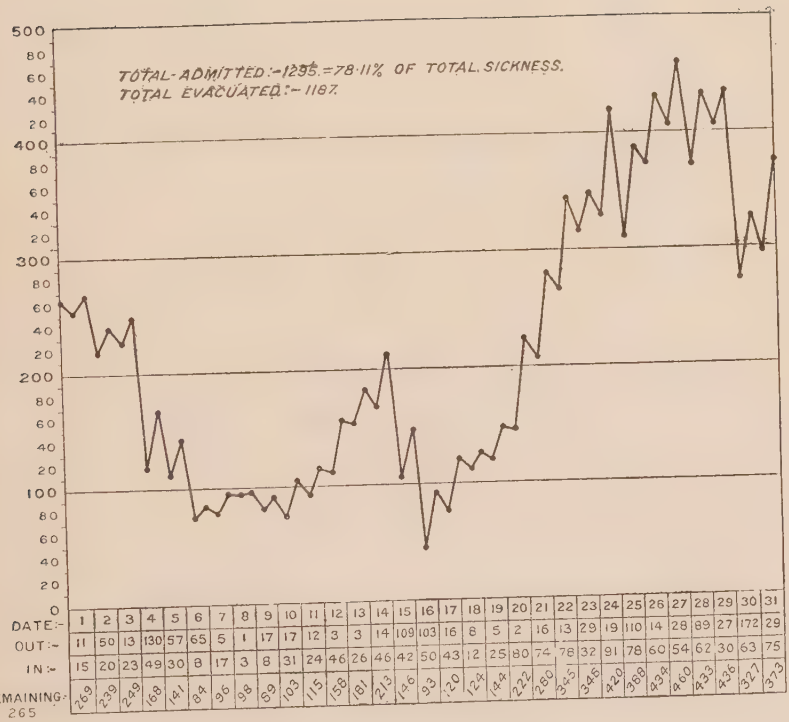
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TOTAL EVACUATED:-1187.
500
400
300
200
100
0
DATE:- 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
OUT:- 11 50 13 130 57 65 5 1 17 17 12 3 3 14 109 103 16 8 5 2 16 13 29 19 110 14 28 89 27 172 29
IN:- 15 20 23 49 30 8 17 3 8 31 24 46 26 46 42 50 43 12 25 80 74 78 32 91 78 60 54 62 30 63 75
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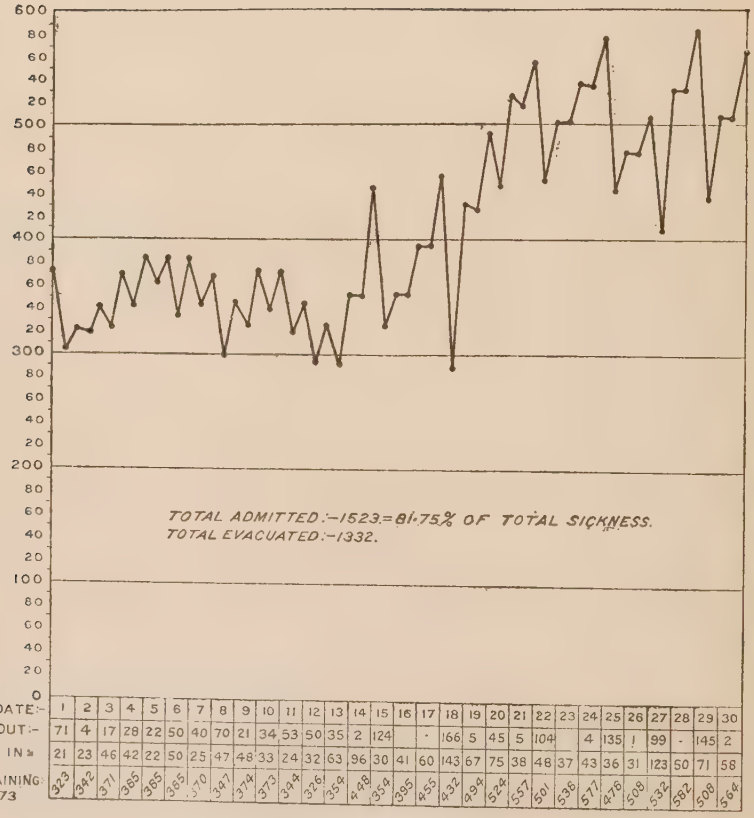
MALARIA, SEPTEMBER, 1917.

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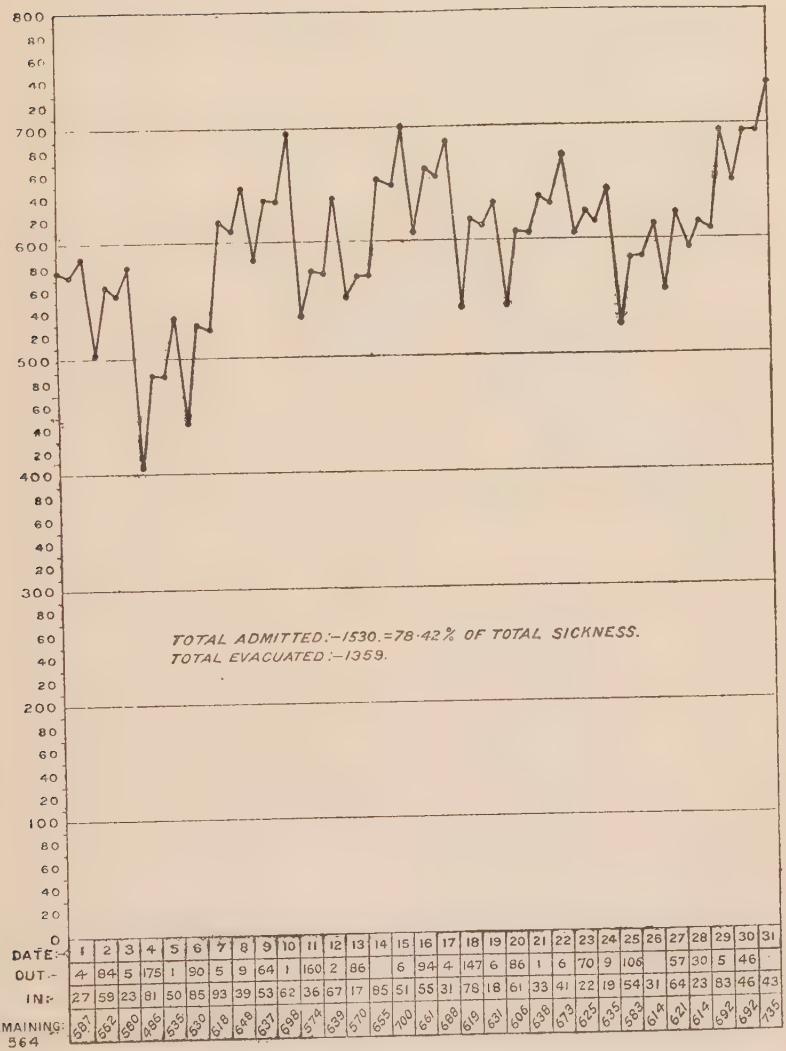
| OUT:- | 71 | 4 | 17 | 28 | 22 | 50 | 40 | 70 | 21 | 34 | 53 | 50 | 35 | 2 | 124 | | · | 166 | 5 | 45 | 5 | 104 | | 4 | 135 | 1 | 99 | - | 145 | 2 |
| IN:- | 21 | 23 | 46 | 42 | 22 | 50 | 25 | 47 | 48 | 33 | 24 | 32 | 63 | 96 | 30 | 41 | 60 | 143 | 67 | 75 | 38 | 48 | 37 | 43 | 36 | 31 | 123 | 50 | 71 | 58 |
| REMAINING: 373 | 323 | 342 | 371 | 385 | 385 | 385 | 370 | 347 | 374 | 373 | 344 | 326 | 354 | 448 | 354 | 395 | 455 | 432 | 494 | 524 | 557 | 501 | 538 | 577 | 476 | 508 | 532 | 582 | 508 | 564 |

## October, 1917.

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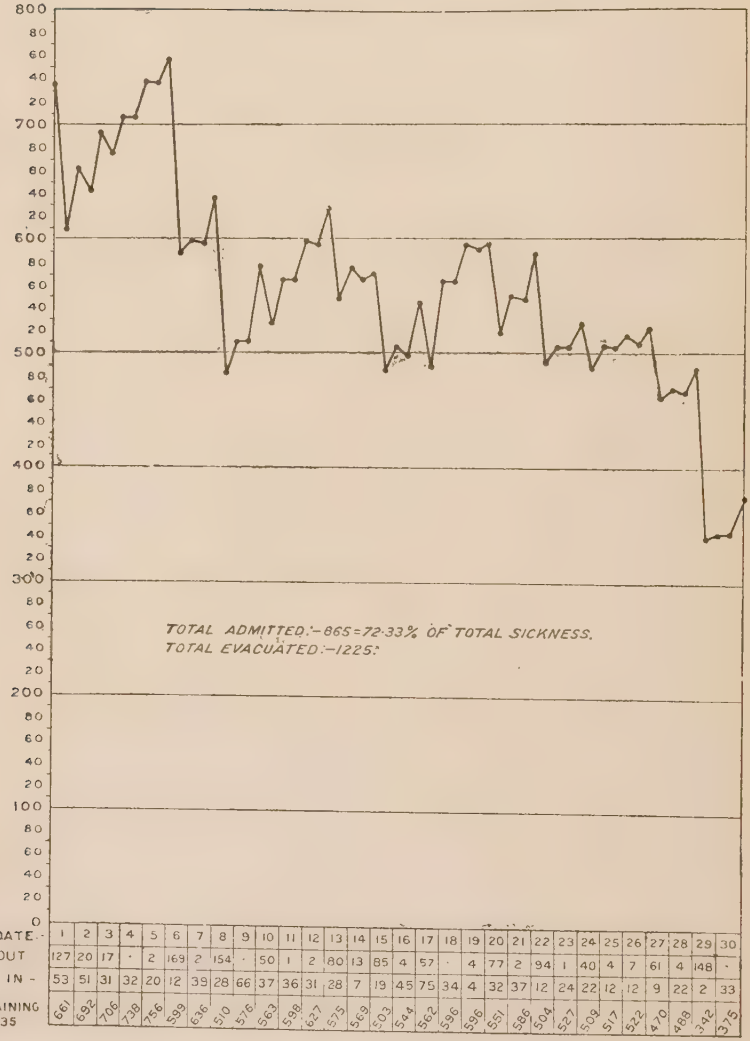
| OUT:- | 4 | 84 | 5 | 175 | 1 | 90 | 5 | 9 | 64 | 1 | 160 | 2 | 86 | | 6 | 94 | 4 | 147 | 6 | 86 | 1 | 6 | 70 | 9 | 106 | | 57 | 30 | 5 | 46 | |
| IN:- | 27 | 59 | 23 | 81 | 50 | 85 | 93 | 39 | 53 | 62 | 36 | 67 | 17 | 85 | 51 | 55 | 31 | 78 | 18 | 61 | 33 | 41 | 22 | 19 | 54 | 31 | 64 | 23 | 83 | 46 | 43 |
| REMAINING: 564 | 587 | 562 | 580 | 486 | 535 | 630 | 618 | 648 | 637 | 698 | 574 | 639 | 570 | 655 | 700 | 661 | 688 | 619 | 631 | 606 | 638 | 673 | 625 | 635 | 583 | 614 | 621 | 614 | 692 | 692 | 735 |

## Malaria, November, 1917.

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| REMAINING 735 | 661 | 692 | 706 | 738 | 756 | 599 | 636 | 510 | 576 | 563 | 598 | 627 | 575 | 569 | 503 | 544 | 562 | 596 | 596 | 551 | 586 | 504 | 527 | 509 | 517 | 522 | 470 | 489 | 342 | 375 |

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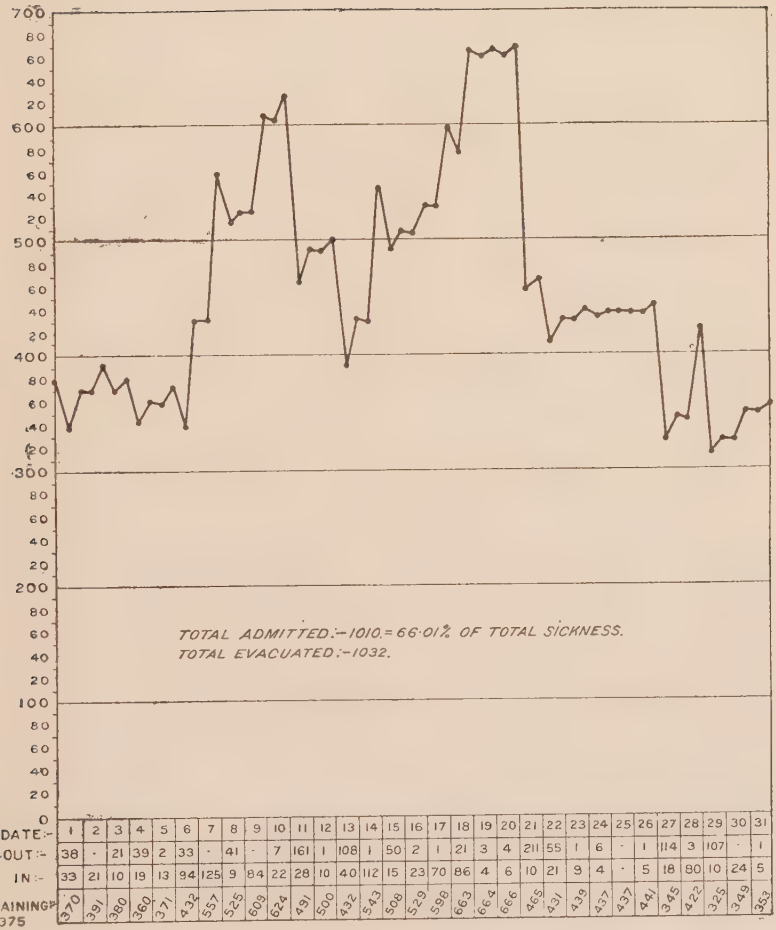


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| OUT:— | 38 | · | 21 | 39 | 2 | 33 | · | 41 | · | 7 | 161 | 1 | 108 | 1 | 50 | 2 | 1 | 21 | 3 | 4 | 211 | 55 | 1 | 6 | · | 1 | 114 | 3 | 107 | · | 1 |
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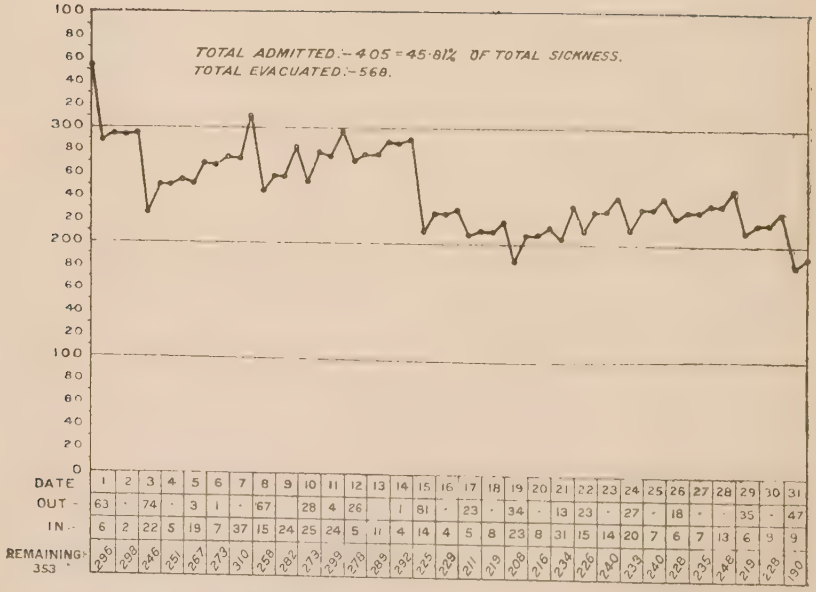
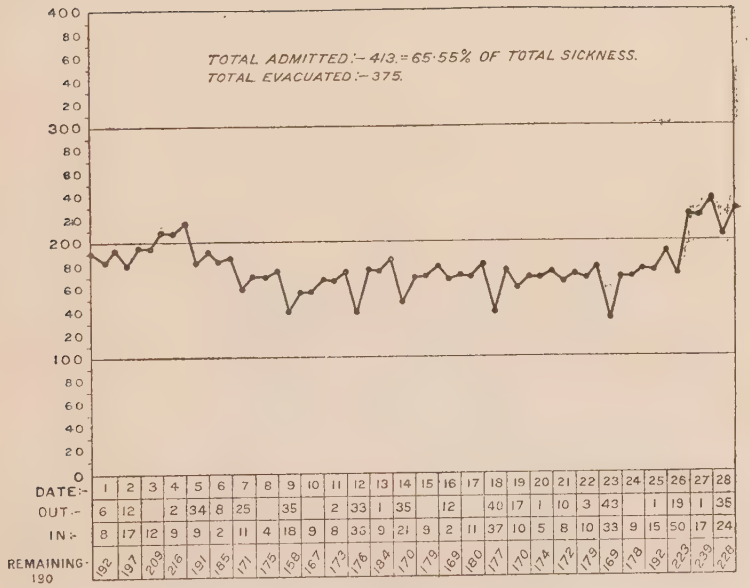
| REMAINING 375 | 370 | 391 | 380 | 360 | 371 | 432 | 557 | 525 | 609 | 624 | 491 | 500 | 432 | 543 | 508 | 529 | 598 | 663 | 664 | 666 | 465 | 431 | 439 | 437 | 437 | 441 | 345 | 422 | 325 | 349 | 353 |

MALARIA, JANUARY, 1918.



## February, 1918.

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| DATE:– | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
| OUT:– | 6 | 12 | | 2 | 34 | 8 | 25 | | 35 | | 2 | 33 | 1 | 35 | | 12 | | 40 | 17 | 1 | 10 | 3 | 43 | | 1 | 19 | 1 | 35 |
| IN:– | 8 | 17 | 12 | 9 | 9 | 2 | 11 | 4 | 18 | 9 | 8 | 36 | 9 | 21 | 9 | 2 | 11 | 37 | 10 | 5 | 8 | 10 | 33 | 9 | 15 | 50 | 17 | 24 |
| REMAINING 190 | 192 | 197 | 209 | 216 | 191 | 185 | 171 | 175 | 158 | 167 | 173 | 176 | 184 | 170 | 179 | 169 | 180 | 177 | 170 | 174 | 172 | 179 | 169 | 178 | 192 | 223 | 239 | 228 |

# INDEX.

ADRENALIN in blackwater fever, 200
Africa, East, medical officers serving in, advantage over those serving in France or at home in knowledge of malarial disease, 248
Algid malaria, symptoms, 33
Amblyopia, due to kidneys' failure to excrete quinine, 219
,, malarial, in pernicious malaria, 33
,, (quinine), 33, 227
,, ,, following blackwater fever, treatment of, 229
,, ,, ,, large doses of quinine in blackwater fever, case, 186
,, ,, in blackwater fever, case, 222
,, ,, pallor of optic discs in, 227
Anæmia, malarial, blood changes in, tabulation, 160
,, ,, causes of, 140
,, ,, colour index in, 158
,, ,, indications of, 140
,, ,, prescription for, 142
,, ,, treatment, 140
,, ,, ,, of, by arsenic, cases illustrating, 151-156
,, ,, ,, of, by galyl, cases, 143-151
,, ,, ,, by quinine, 158
,, pernicious, and malaria, 159
,, ,, ,, blood films, 164, 165, 167
,, ,, ,, post-mortem report of case, 169
,, ,, ,, symptoms, case illustrating, 163
,, ,, blood changes in, tabulation of, 159
,, ,, invariable fatality of, 159
,, post-malarial symptoms, case illustrating, 173
,, ,, treatment by galyl: recovery, 172
,, profound, case, 161
,, ,, post-mortem report, 163
,, ,, symptoms, 161
Anopheles, description of, 3, 4
,, larvæ and pupa of, 4
Anti-malaria officers, 22
,, ,, work of, on the Struma, 22
,, squads, duties of, in prevention of malarial fever on the Struma, 22
Appendicitis complicating malaria, 249
,, ,, ,, necessity for prompt operation in, 250

Appendicitis malarial, described as clinical entity, 249
Apyrexial interval in malarial fever (benign tertian), quinine in, 27
Arsenic and iron in pernicious malaria, 106
,, ,, ,, in combination with quinine in malaria, success of, 137
,, and quinine in malarial anæmia, 176
,, by mouth, and galyl in malarial anæmia, relative value of, 143
,, ,, ,, in malaria anæmia, 142
,, in malarial anæmia, cases illustrating treatment, 151-156
,, in pernicious anæmia and malaria, case, 168
,, in post-malarial anæmia, 172
,, in recurrent malaria with jaundice, case, 112
,, tonic in convalescence of malarial hæmoglobinuria and blackwater fever, 229
,, ,, in malarial tremor case, 241
,, value of, in post-malarial anæmia, estimate of, 156

Benign tertian malaria, 5, 26
Bilious malarial fever with extreme jaundice; vomiting and hiccough successfully treated with large doses of quinine, case, 118
,, remittent fever, characteristics of, 115
,, ,, ,, quinine in, scale of doses of, 124
,, ,, ,, with cerebral complications, death from, case, 115
,, ,, ,, ,, ,, post-mortem report, 11
Bivouac nets, 22
,, ,, how rendered non-inflammable, 24
,, ,, method of using, 23
,, ,, surprise inspection of, 23
,, ,, use of, on the Struma in prevention of malaria, 22
,, ,, ,, ,, ,, ,, inspection of, 22
,, ,, ,, ,, ,, ,, precautions against fire, 24

Blackwater fever, ætiology, 182
,, ,, ,, case, 210
,, ,, complication of malaria, 180
,, ,, deaths from, post-mortem report, 201, 218, 233
,, ,, distinction of, from malarial hæmoglobinuria and quinine hæmoglobinuria, 180
,, ,, occurrence of, only in malarial subjects, 182
,, ,, predisposing causes, 183
,, ,, quinine in, dosage, 228, 229
,, ,, not treated with quinine, death from, case illustrating, 230, 231
,, ,, not treated with quinine, death from, post-mortem, 233
,, ,, recovery from, case, 183, 193, 204, 210, 220
,, ,, symptoms in, 180
,, ,, cases illustrating, 183, 193
,, ,, toxæmia of, affecting kidney, 181
,, ,, treatment, case illustrating, 183
Bladder and kidney, epithelial cells from, in Blackwater fever, case, 185, 234

Blindness following pernicious forms of malaria, 33
Blood changes in malarial anæmia, tabulation, 160
,, ,, pernicious anæmia, tabulation, 159
,, corpuscles, red, action of benign tertian parasites on, 11
,, ,, ,, ,, malignant malarial parasites on, 11
,, ,, ,, destruction by malarial parasites, 10
,, culture, technique of taking blood for, 255
,, film in Blackwater fever, case, 185, 188, 189, 190
,, ,, case of pneumonia complicating malaria, 251
,, ,, pernicious anæmia and malaria, case, 164, 165, 167
,, ,, profound anæmia, case, 161, 162
,, ,, case of pernicious anæmia and malaria, 168
,, ,, malaria, examination, 37
,, ,, ,, preparation and staining, points of importance in, 14
,, ,, ,, ,, technique, 13, 14
,, ,, which no parasites were found, explanation, 37, 38
,, film, necessity of, in suspected cases of malaria, 55
,, great destruction of, in pernicious malaria cases, 112, 172
,, normal, leucocytes in, 160
,, transfusion of, in pernicious anæmia and malaria, case, 168
Brandy and chlorodyne with castor oil in malarial diarrhœa, 55
,, in Blackwater fever, 195
British Isles; probabilities of outbreak of malaria after the war, 139
Bush and undergrowth, destruction of, on the Struma in prevention of malaria, 25

Cachexia, malarial, 176
,, ,, symptoms, 176
Calomel and sulphate of magnesia in malarial cachexia, case, 177
,, in Blackwater fever, 183, 189, 195
,, in malaria, 55
,, in myoclonus in recurrent malaria, 243
,, in redwater fever, 235
Castor oil with chlorodyne and brandy in diarrhœa of malaria, 55
Cerebral complications in bilious remittent fever, death from, case, 115
,, malaria and cerebrospinal meningitis, value of quinine in diagnosing between, case, 92
,, ,, cases, 38
,, ,, clinical aspect of, 32
,, ,, death from, cases of, 57, 62, 67
,, ,, ,, ,, *post-mortem* reports, 58, 59, 65, 71
,, ,, pathology, 31, 32
,, ,, recovery after attack of, case, 60, 72, 78, 84, 89, 95
,, ,, ,, from, cases illustrating treatment by large doses of quinine, 72, 78, 84, 89, 95
,, ,, symptoms, 32, 56
,, ,, ,, onset, 56
,, ,, treatment by quinine in large doses, recovery, 60, 61, 77, 82, 87, 91, 94, 99

Cerebral malaria, treatment by quinine, scale of doses, 100
,, ,, ,, resulting in death, case, 58, 65, 71
,, ,, ,, of, routine, 55
Chlorodyne and brandy with castor oil in diarrhœa of malaria, 55
Climate, change of, need of, for malarial patients, 134
Cold and fatigue predisposing causes in blackwater fever, 183
Colitis, mucous, malarial, 254
Colour index in malarial anæmia, 158
Coma and semi-coma, differential diagnosis, means of making, 32, 53, 92, 256
Creosote mixture, in case of pneumonia complicating malaria, 251, 253
Cresol, deadly effect of, on mosquito larvæ and pupæ, 21
Culex, description of, 5

"DANGEROUSLY ill list," number of malarial patients on, 38
Deafness in quinine treatment, bromides in, 132
Dengue fever, mosquitoes transmitting, 3, 5
Diarrhœa (malarial), castor-oil with chlorodyne and brandy in, 55
Digitaline and strychnine in pernicious anæmia and malaria, case, 165
,, ,, in profound anæmia, case, 162
,, in blackwater fever, case, 188, 199
,, in case of pneumonia complicating malaria, 251, 252
Drainage, successful, of village 100 miles from Salonika, in prevention of malaria, method, 17
Dug-outs, whitewashing of, 24
Dysentery complicating malarial fever, 254
,, (hospital), 254

ENTERIC group of fever, diagnosis from malaria, 254, 255
Epithelial cells from bladder and kidney in blackwater fever, case, 195, 234
,, ,, in urine in redwater fever, case, 234, 236
Epithelium, urinary, destruction of, in blackwater fever, case, 204

GALYL and arsenic by mouth in malarial anæmia, relative value of, 143, 156
,, ,, in malarial anæmia, 140
,, ,, ,, ,, relative expense of, 157
,, in malarial anæmia, 140; cases illustrating treatment, 143-151
,, in profound anæmia, case, 162
,, pernicious anæmia and malaria, 165
,, intravenous injection in convalescent stage of malarial hæmoglobinuria and blackwater fever, 229
,, reaction of temperature to, in treatment of malarial anæmia, 151
,, solution in malarial anæmia, technique for administration, 142
,, ,, preparation, 140
Glomeruli, cessation of action of secretory cells in blackwater fever, 181
Gloves, obligatory use of at night on the Struma in prevention of malaria, 24
Granular casts in urine in redwater fever, case, 235
,, deposits in urine in blackwater fever, case, 180, 195, 197
Gum solution, alkaline, intravenous injections of, in blackwater fever, 182

Hæmoglobinuria and Blackwater fever, 180
,, ,, malarial fever, cause of, 11
,, malarial, colour of urine in, 180
,, ,, scale of doses of quinine in, 229
,, ,, see also *Red-water fever*.
,, quinine, 180
Hæmolysin, production in malarial fever, 11
Hæmorrhages, petechial, in cerebral malaria, causes of, 30
Head nets, provision of, on the Struma, in prevention of malaria, 24
Heart, effect of malaria parasites and toxins upon, 110
,, muscle, effects of toxins of malaria upon, 102
,, ,, weakening of, in chronic malaria, 253
,, symptoms, and collapse in pernicious malaria, case, 102
,, post mortem appearance in case of blackwater fever, 218
Hiccough, vomiting and jaundice in bilious malarial fever, treatment with large doses of quinine, 118
Houses and huts, mosquito-proof, 16
Huts, whitewashing of, in destruction of mosquitoes, 24

Intramuscular injection of quinine, 39, 41,
Intravenous injection of quinine, 39, 42, 43, 44, 45, 46
Iron and arsenic combined with quinine in malaria, success of, 137
,, ,, in pernicious malaria, 106

Jaundice in recurrent malaria treated with large doses of quinine, case, 112
,, vomiting, and hiccough in bilious malarial fever, treated successfully with large doses of quinine, case, 118

Kidney and bladder, epithelial cells from, in blackwater fever, case, 195
Kidneys, malarial changes in, 13
,, post mortem appearances in blackwater fever, 219
,, affected by toxæmia in blackwater fever, 181

Laparotomy in acute hæmorrhagic pancreatitis in pernicious malaria, case, 111
Latent malaria, treatment, 34
Laveran, discovery of parasite of malaria by, 1
Leucocytes in normal blood, 160
Liver in blackwater fever, post mortem appearances, 202, 219, 233
,, malarial changes in, 13
Lumbar puncture in diagnosis in cases of coma and semi-coma, 32, 53, 92, 256
,, ,, malaria, technique, 53, 54

Macedonia, medical officers serving in, advantage over those serving in France or at home in knowledge of malarial disease, 248
,, malarial fever in, 2, 3
,, ,, ,, reduction of mortality, 36
,, ,, ,, treatment, 35

Macedonian swamps, extensive schemes for drainage of, 17
Macrogametes, 6, 7
Macrogametocytes, 6, 7, 10
Magnesia, sulphate of, and quinine in malaria, 55
,, ,, ,, calomel in malarial cachexia, case, 177
Malarial drainage of swamps in Macedonia, 17
,, fever, action of quinine in, 11
,, ,, acute, three stages of, 26
,, ,, ,, clinical features of, 26
,, ,, and peripheral neuritis, case of, clinical description, 244
,, ,, ,, ,, ,, ,, post-mortem examination, 245
,, ,, ,, ,, ,, ,, sections of tissue, Base Laboratory report on, 245
,, ,, ,, ,, ,, ,, treatment, 245
,, ,, appendicitis complicating, 249
,, ,, chronic, treatment, 126
,, ,, ,, insufficiently treated with quinine, main feature of blackwater fever, 203
,, ,, ,, weakening of heart muscle in, 110, 253
,, ,, climatology, 2
,, ,, complicated by dysentery, 254
,, ,, common-sense precautions against, 17
,, ,, complicated by pneumonia, case, 250
,, ,, diagnosis of enteric group of fever from, 254, 255
,, ,, effect of, on central nervous system, and on peripheral nerves, 240
,, ,, hæmoglobinuria in case of, 11, 180, 233
,, ,, height of temperature and severity of attack, upon what dependent, 10
,, ,, history, 1
,, ,, in Macedonia, 2, 3
,, ,, incubation period, 10
,, ,, neglected (blackwater fever), death from, 197, 213, 219, 230
,, ,, parasites of, 5
,, ,, ,, life cycle in mosquito (sporogony) and in man (shizogony), 6
,, ,, ,, destruction of red blood corpuscles by, 10
,, ,, ,, discovery, 1, 2
,, ,, ,, ,, developmental cycle in mosquito, 2
,, ,, ,, ring forms of, 10
,, ,, ,, toxins produced by, 11
,, ,, ,, type of, 10
,, ,, pathology of, 12, 31
,, ,, pernicious manifestations of, 30
,, ,, production of hæmolysin in, 11
,, ,, prophylaxis, 16
,, ,, symptoms, cause of, 10
,, ,, treatment, 35
,, ,, ,, routine, 55

Malarial tremor, case, 240, 241
,, ,, symptoms, case, 241
Malignant tertian malaria, 5, 29
Medical officers at the Struma front, small experience of, in malaria, 135
Meningitis, cerebrospinal and cerebral malaria, value of quinine in diagnosing between, case, 92
Menstruation, effect of quinine upon, 134
Mesopotamia, medical officers serving in, advantage over those serving in France or at home in knowledge of malarial disease, 248
Microgametocytes, 6, 7, 10
Mortality from malaria, reduction, 36
Mosquito, developmental cycle of parasite of malaria in, discovery, 2
,, nets, in prophylaxis against malaria, 16, 17, 22
,, proof houses and huts in prevention of malarial fever, 16, 24
Mosquitoes, destruction of, on the Struma, by antimalarial squads, 22
,, larvæ and pupæ, effect of cresol on, 21
,, ,, destruction in prevention of malarial fever of, 24
,, ,, of, effect of paraffin and green tar oil upon, 20
,, transmitting malaria, 3
Musculo-spiral paralysis following intramuscular injection of quinine, 42
Myoclonus in malaria, recurrent, case, 242
,, recurrent malaria, symptoms, 242

Nerves, peripheral effect of malaria upon, 240
Nervous system, central, disturbance in malaria, method of quinine, administration for, 42, 43
,, ,, ,, effect of malaria upon, 240
,, symptoms, obscure, in malarial patients, 32
Neuritis, brachial, complicating case of malignant tertian malaria, 246
,, complicating malaria, diagnosis, 247
,, peripheral, in malaria, case, 243
Nux vomica, tincture, in case of malaria and peripheral neuritis, 245

"Oil Drip," method for slowly running water in prevention of malarial fever, 21
Optic discs, pallor of, in quinine amblyopia, 34, 227
Oxalate crystals in urine in redwater fever, case, 235

Pancreatitis, acute hæmorrhage in pernicious malaria, case, 111
Paraffin and green tar oil in spraying pools in prevention of malarial fever, 20; on the Struma, 24
,, on surface of pools, effects of on mosquito larvæ, 20
,, spraying of, over pools in prevention of malarial fever, 20; on the Struma, 24
Parasites and toxins (malaria), effect of, on heart, 110
,, malarial, absence from blood films on examination, explanation, 37, 38. See also *Malarial fever*, parasites of
Paratyphoid fever, diagnosis from malaria, 255
Pernicious malaria, acute hæmorrhagic pancreatitis in, case, 111

Pernicious malaria, deaths from heart failure, cases, 106, 109, 110
,, ,, ,, ,, ,, ,, post-mortem report, 108, 109, 110
,, ,, with cardiac symptoms and collapse, 102
,, ,, maximum dose of quinine in, 123, 228
Pituitrin in blackwater fever, case, 186
,, in profound anæmia, case, 163
*Plasmodium falciparum* (*Laverania*), life cycle, 9
,, ,, ,, malignant tertian (malarial fever) due to, 29
,, ,, ,, parasite of malignant tertian or sub-tertian malaria, 5
,, ,, ,, schizogony in, 9
,, *malariæ*, parasite of quartan malaria, 5, 27
,, ,, life cycle, 8
,, ,, schizogony in, 8
,, *vivax*, parasite of benign tertian malaria, 5, 26
,, ,, life cycle, 9
,, ,, schizogony in, 9
Pneumonia complicating malaria, case, 250
,, ,, ,, ,, clinical reports, 250, 251, 252, 253
,, ,, ,, ,, treatment, 251, 252, 253
Potassium, bromide of, in malarial tremor, case, 241

QUARTAN fever and benign tertian (malarial fever), resemblance between, 29
,, ,, blood films examined, 37
,, ,, parasite of, 5, 8
,, ,, prodromata, 28
,, ,, rare type of malarial fever, 27
,, ,, stages in, 28
Quinine, action in malarial fever, 11
,, administered intramuscularly and by mouth, in case of pneumonia complicating malaria, 251, 252, 253
,, administration in malaria by intramuscular injection, accidents following, 42
,, ,, ,, ,, ,, indications for, 42
,, ,, ,, ,, ,, method and precautions in, 41
,, ,, ,, by intravenous injection, 42, 43
,, ,, ,, ,, ,, apparatus for, 43
,, ,, ,, ,, ,, dangers, 46
,, ,, ,, ,, ,, indications for, 42, 43
,, ,, ,, methods, 39
,, ,, ,, oral, forms of, 39
,, ,, ,, ,, in solution, 40
,, ,, ,, ,, in tablet form, valueless, 40
,, ,, ,, ,, powdered, 40

Quinine administration in malaria, oral, rectal, 53
,, ,, intramuscular, in blackwater fever, case, 183
,, ,, intravenous, in pernicious malaria, with cardiac symptoms, case, 104
,, and arsenic in malarial cachexia, 176
,, and sulphate of magnesia in malaria, 55
,, average dose of, in chronic malaria, 127
,, bihydrochloride, dosage, 39
,, ,, intravenous injection, technique for, 44, 45
,, ,, ,, ,, precautions in, 45, 46
,, ,, value of, 40
,, combined with arsenic and iron in malaria, success of, 137
,, effect of, in menstruation, 134
,, ,, on uterus, 134
,, hydrochloride, 39
,, in bilious remittent fever, effects of, 115, 118
,, in blackwater fever, 182
,, ,, ,, caution in administration, 228
,, ,, ,, cumulative effect, 228
,, ,, ,, importance of, 192
,, ,, ,, maximum dosage, 228
,, ,, ,, scale of doses in, 229
,, in chronic malaria, 126
,, ,, ,, statistics of seventy-seven hospital ship cases, 126
,, in large doses in bilious malarial fever with jaundice, vomiting, and hiccough : recovery, 118
,, ,, ,, in blackwater fever, case, 185
,, ,, ,, in diagnosis of coma and of semi-comatose cases, 256
,, ,, ,, intravenous and intramuscular method in cerebral malaria, statistics of results, case, 56, 60
,, ,, ,, in cerebral malaria, cases illustrating success of, 72, 99
,, ,, ,, in malaria, arguments advanced against, 131
,, ,, ,, ,, death preventable by, 129
,, ,, ,, in malarial cachexia, case, 178
,, ,, ,, in recurrent malaria, with jaundice, case, 112
,, in chronic malaria dosage, 131, 137
,, ,, ,, duration of treatment, 130
,, ,, ,, method of treatment, 136
,, ,, ,, quantity necessary for cure, 131
,, in malarial anæmia, 140, 158
,, ,, hæmoglobinuria and blackwater fever, scale of doses, 229
,, ,, tremor, 240
,, in myoclonus in recurrent malaria, 243
,, in pernicious anæmia and malaria, case, 176
,, ,, ,, maximum dose, 228
,, in post-malarial anæmia, case, 174
,, in prevention of reinfection of malaria, 138
,, ,, of secondary attack of malaria after apyrexial attack, 27, 30

Quinine in profound anæmia, case, 161
,, in prophylaxis of malarial fever, 16
,, ,, ,, ,, failure, 16
,, in redwater fever, 235
,, insufficient doses of, in malaria, resulting in blackwater fever, 203, 219
,, salts of, available in, treatment of malaria, 39
,, sulphate of, 39, 40
,, ,, in blackwater fever, case, 182, 183
,, ,, in malarial cachexia, case, 177
,, toleration, 132
,, value of, in differential diagnosis between cerebral malaria and cerebrospinal meningitis, case, 92
Quotidian fever, 5

Recurrent malaria with myoclonus, case, clinical description, 243
" Redwater fever," colour of urine in, 180, 233
,, ,, symptoms, 234
,, ,, treatment, 229, 239
Retinal arteries, narrowing of, in quinine amblyopia, 34, 227
Ross, Sir Ronald, F.R.S., discovery of developmental cycle of parasite of malaria in mosquito, 2
Ross, Sir Ronald, F.R.S., 184, 192

Saline in blackwater fever, 182
,, intravenous injection in malaria, danger of, in large doses, 46-52
,, ,, ,, ,, deaths from, with case histories, 46-49
,, rectal injection in blackwater fever, 188, 195, 199, 229
,, ,, ,, in malaria cachexia, case, 178
,, ,, ,, in pernicious anæmia and malaria, case, 165
,, ,, ,, in redwater fever, case, 229, 235
,, ,, ,, with quinine in post-malarial anæmia, case, 174
,, ,, ,, ,, in profound anæmia, case, 162
Schizogony, 8
,, in *Plasmodium falciparum* (*Laverania*), 9
,, ,, *malariæ*, 8
,, ,, *vivax*, 9
Sciatic palsy following intramuscular injection of quinine, 42
Soda, bicarbonate of, and quinine, relative value of, in blackwater fever, case illustrating, 192
,, ,, in blackwater fever, case, 184
Sodium sulphate and quinine in malignant tertian malarial fever with blood and mucous in stool, 30, 254
Spleen, enlarged or tender in malaria, quinine in, 55
,, malarial changes in, 13
,, post-mortem appearances in blackwater fever, 202, 219, 233
Sporoblasts, 6, 7,
Sporogony, sexual cycle in female anopheline, 6
Sporozoites, 6, 7, 8
Stagnant water, drainage of, in prevention of malarial fever, 17; on the Struma, 24

Stegomyia, description of, 5
Stewart, Col. Purves, note on case of malaria and peripheral neuritis, 244
,, ,, ,, malignant tertian malaria with right brachial neuritis, 247
,, ,, ,, recurrent malaria, with myoclonus, 243
Stools, cultivation of bacillus from, in diagnosis of enteric and paratyphoid fevers, 256
Struma Front, chronic malaria on, 135
,, Valley, anti-malaria precautions in, 21
Strychnine and digitaline in pernicious anæmia and malaria, case, 165
,, ,, ,, profound anæmia, case, 162
,, in blackwater fever, cases, 188, 199
,, ,, case of pneumonia complicating malaria, 251, 252
,, ,, quinine amblyopia following blackwater fever, 229
Swamps, drainage of, in prevention of malarial fever, 17
,, method of filling in where drainage impossible, 20

Tanks, &c., spraying of, with paraffin in prevention of malarial fever, 21
Tar oil, green, and paraffin for spraying pools in prevention of malarial fever, 20; on the Struma, 24
Temperature, reaction of, to galyl in treatment of malarial anæmia, 151
Tertian benign malarial fever, blood films examined, 37
,, ,, ,, most common type of malarial fever, 26
,, ,, ,, parasite of, 5, 9
,, ,, ,, parasites of, effect on red cells, 11
,, ,, ,, prodromata, 26
,, ,, ,, symptoms, 26
,, ,, ,, stages in, symptoms, 27
,, (malignant), malarial fever, 29
,, ,, ,, ,, blood films examined, 37
,, ,, ,, ,, gametocytes, parthogenesis, 10
,, ,, ,, ,, large doses of quinine required in, 129
,, ,, ,, ,, prodromata, 29
,, ,, ,, ,, stages in, 29
,, ,, ,, ,, with right brachial neuritis, case, 246
,, or subtertian (malignant), malarial fever, action on red corpuscles, 11
,, ,, ,, ,, ,, parasite of, 5, 9
Theatres, open-air, malarial fever, spread by, 17
Toxins and parasites (malaria), effects of, on heart, 110
,, produced by malarial parasites, 11
Trophozoites, 7, 8
Typhoid fever, diagnosis from malaria, 255

Urine, change of colour in, relation of to amount of debris, epithelial cells, and casts in, 209
,, colour of, in blackwater fever, 180, 194
,, ,, ,, redwater fever, 180, 233
,, deposits of, in redwater fever, and blackwater fever, comparison between, 234

Urine, granular deposits in, in blackwater fever, case, 195
,, in redwater fever, laboratory reports, case, 235, 236, 237
,, quantity passed in blackwater fever, indication of size of dose of quinine, 228
,, suppression of, in blackwater fever, causes of, 181
Uterus, effect of quinine upon, 134

Vision, contractions of, fields of, in quinine amblyopia, 227, 228
,, no change in, after recovery from quinine amblyopia, 227
Vomiting in malarial tremor, case, 241
,, in redwater fever, case, 236

Whitewashing of interior of dugouts and huts on the Struma, in prevention of malaria, 24
Widal reaction, technique of taking blood for, 255
Women suffering from malaria, treatment of, 134

Zygotes, 6, 7

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